ExxonMobil Chemical Company

Alkyl Alcohols C6 to C13 Category Analysis Report

For the

U.S. High Production Volume Chemical Challenge Program

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EXECUTIVE SUMMARY

ExxonMobil Chemical Company hereby submits the category summary report for Alkyl Alcohols C6 - C13 Category under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program (Program). The purpose of this report is to:

- Present results of an assessment to determine whether seven complex mixtures can be adequately characterized with existing data and additional data as described in the Alkyl Alcohols C6 - C13 Category test plan.
- Summarize the SIDS (Screening Information Data Set) physicochemical, environmental fate and effects, and human health HPV Program endpoints for the Alkyl Alcohols C6 - C13 Category.
- Provide a description of manufacturing processes, potential exposure sources, and uses for C6 - C13 Alkyl Alcohols.

The Alkyl Alcohols C6 to C13 Category is a family of saturated alcohols that are produced from olefins by the hydroformylation or "oxo" process. Hydroformylation is the reaction of an olefin with carbon monoxide and hydrogen to produce an aldehyde, and its subsequent hydrogenation to the alcohol. The number of carbon atoms in the category members ranges from 6 to 13. Category members contain predominantly branched alkyl groups. Each substance consists of an isomeric mixture of saturated primary alcohols of high purity, and the following basic structure: CH_3-R-CH_2-OH, where R is a branched isomeric structure.

The justification for the Alkyl Alcohols C6 to C13 Category is that the members have:

- similar chemical structures,
- similar physico-chemical properties,
- comparable environmental fate,
- the same mode of action.

In general, the acute aquatic toxicity of aliphatic alcohols occurs by non-polar narcosis (Lipnick *et al.*, 1985). The mode of action is disruption of biological membrane function (van Wezel and Opperhuizen, 1995). Mammalian metabolic pathways for both linear and branched n-primary alcohols are likely to include similar reactions for all category members and result in structurally similar metabolites (carboxylic acids).

The data demonstrate that the category is valid for a screening-level hazard assessment for the category and its members (CAS numbers, 68526-79-4, 70914-20-4, 68526-83-0, 28473-21-4, 68526-84-1, 68526-85-2, and 68526-86-3). One can assess the untested endpoints by extrapolation between and among the category members. Details are given in the subsequent chapters.

Exposure

Alkyl Alcohols C6 to C13 Category substances are primarily used as chemical intermediates and additional applications can include uses such as co-solvents, anti-foaming agents, solvent extraction and flotation. Based on physical properties, the primary workplace exposure would be through inhalation and dermal contact. The majority of the applications do not contain free alcohols; therefore, minimal consumer exposure is foreseen, since the consumer is only indirectly exposed through the use of the applications and uptake is expected to be low.

At production sites, potential exposure to Alkyl Alcohols C6 to C13 in the environment is low because there are no direct releases to the environment and process, storage, and handling facilities are enclosed.

Based on the physico-chemical properties of category members, Alkyl Alcohols C6 to C13 at equilibrium in the environment will partition mainly to water (C6 to C10) with a shift to the sediment compartment as carbon chain length increases (C13).

Human Health

Members of the Alkyl Alcohols C6 to C13 Category have a low order of toxicity by the oral, dermal, and inhalation routes of exposure. Oral LD_{50}s ranged from >2000-3900 mg/kg and dermal LD_{50}s ranged from >2600-3160 mg/kg. Inhalation exposure studies were generally conducted at the maximally attainable vapor concentrations, and animals generally showed no signs of toxicity other than CNS depression. LC_{50}s were therefore >1060 ppm for the lighter C6 alcohols, and >12 ppm for the heavier C13 alcohols. Thus, acute toxicity for the Alkyl Alcohols C6 to C13 Category has been well characterized and no further studies are proposed.

Members of the Alkyl Alcohols C6 to C13 Category are mildly to markedly irritating to the skin and mildly to severely irritating to the eyes. Additionally, Alcohol C9-11-iso, C10 rich produced moderate upper airway sensory irritation in male mice exposed to vapor atmospheres ranging from 111 to 168 ppm. Thus, the skin, eye, and respiratory tract irritation potential for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

Members of the Alkyl Alcohols C6 to C13 Category are not expected to be skin sensitizers in animals or humans. A structurally similar chemical, 1-hexanol, did not induce sensitizing reactions in guinea pigs or humans. Data were not available to assess the potential for respiratory tract sensitization in animals or humans, however, since they are not expected to be skin sensitizers, it is not expected that category members would cause respiratory sensitization. Additionally, due to the low vapor pressure of members of this category, atmospheric exposure is expected to be low. Although limited data are available to characterize the sensitization potential for the Alkyl Alcohol C6 to C13 Category, the irritant properties of these chemicals make further testing a low priority and no further studies are proposed.

Category members are expected to have a low order of subchronic toxicity. In comparative screening studies designed to evaluate the liver and testes, repeated oral doses of iso-nonanol, iso-decanol, and tridecanol for 14-days produced minimal hepatotoxic effects and no testicular effects in rats. No Observable Adverse Effects Levels (NOAEL) for the three materials were 144, 168, and 184 mg/kg/day, respectively. In other studies, repeated oral and dermal dosing of nonyl alcohol, produced a low order of toxicity in rabbits. Additionally, a combined repeated dose and reproductive / developmental toxicity screening study was conducted for 14 days using 1-dodecanol in rats. No effects on target organs were reported at the highest dose of 2000 mg/kg/day. In developmental toxicity studies with repeated dosing of the dams, the primary effects were reported to be CNS depression at the higher dose levels. Based on the results of the repeated-dose studies conducted in animals, the members of the Alkyl Alcohols C6 to C13 Category appear to have a low order of subchronic toxicity and no further studies are proposed.

Studies carried out in accordance with OECD test guideline 471, employing *Salmonella typhimurium* have not given any indications of genotoxic effects, either with or without metabolic activation. In

another *in vitro test*, a chromosomal aberration assay using Chinese hamster ovary cells, no mutagenic effects were found with and without metabolic activation. Additionally, i*n vivo* bone marrow micronucleus assays conducted in mice and rats showed no mutagenic effects. Based on the findings of these studies, the members of the Alkyl Alcohols C6-C13 Category showed no mutagenic activity with or without metabolic activation. Thus, the mutagenic potential for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

Developmental toxicity studies conducted by the oral route on alcohols, C7-C9-iso, C8 rich and isononyl alcohols produced consistent results and demonstrated that these materials do not affect reproductive parameters. Although a slight increase in resorptions was observed in the studies, this only occurred in the highest dose group(s) and in the presence of overt maternal toxicity. As supporting information, testing of 1-dodecanol in a combined repeated dose developmental /reproductive study showed no effects to parents or offspring. Furthermore, inhalation exposure to saturated vapors of the linear alcohols, 1-hexanol and 1-octanol, did not induce any statistically significant changes in reproductive parameters. In the subchronic studies of isononyl alcohol and isodecyl alcohol, no changes in testicular weight were observed. These data support the conclusion that members of the Alkyl Alcohol C6 to C13 Category are not selective reproductive toxicants. Thus, the reproductive toxicity for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

In conclusion, members of the Alkyl Alcohol C6 to C13 category have a low order of acute toxicity, are not expected to skin or respiratory sensitizers, but have shown irritant effects to the skin, eyes, and upper respiratory tract. Subchronic studies have also shown a low order of toxicity. Although some slight effects in the liver were seen at high doses, these are likely the result of peroxisome proliferation and thus, do not pose a significant risk to humans. Testing in a variety of genotoxicity assays has not shown any mutagenic activity with or without metabolic activation. Based on the negative genotoxicity data, category members are expected to have a low potential for carcinogenicity. Reproductive/ developmental testing has shown fetal effects in some studies, but only at doses that produced overt maternal toxicity. The data support that members of the category are not selective reproductive toxicants.

Environment

Results of the Mackay Level III environmental distribution model suggest a high environmental distribution into the water compartment for alcohols with a carbon chain length of C6 to C10. The model also predicts a high environmental distribution into the sediment compartment for alcohols C11-C14-iso, C13 rich. Volatilization to the air from aqueous and terrestrial habitats will be negligible because Alkyl Alcohols C6 to C13 have low vapor pressure (<2.59 hPa at 25° C). Indirect photo-degradation of Alkyl Alcohols C6 to C13 Category substances can occur at a rapid rate, however, based on their low vapor pressure it is not expected to contribute significantly to their degradation in the environment. Aqueous photolysis and hydrolysis are also not expected to contribute to the transformation of the alkyl alcohols in aquatic environments because they are either poorly or not susceptible to these reactions.

Biodegradability of the alkyl alcohols has been evaluated with standard 28-day test guidelines. The results from these studies suggest that the alkyl alcohols are subject to microbial degradation under aerobic conditions and are either readily biodegradable or rapidly biodegrade.

The predominant mechanism accounting for removal in a wastewater treatment facility is biodegradation, followed by partitioning to sludge, with volatilisation accounting for the remaining loss.

Member substances of the Alkyl Alcohols C6 to C13 Category have been shown to exhibit moderate to high acute aquatic toxicity. This assessment is supported by the results of aquatic toxicity studies for various organisms covering the three trophic levels. Experimental acute toxicity values for fish and invertebrates range from 0.42 to 97.7 mg/L, and 0.71 to >63 mg/L, respectively. For algae, the experimental 72-hr EC_{50} ranges from 2.6 to 89.0 mg/L. Experimental chronic toxicity data for category members are not available. Calculated chronic toxicity values range from 16.1 to 0.03 mg/L for the three trophic levels.

Category members have a low potential to bioaccumulate in aquatic species based biochemical evidence of biotransformation and on experimentally derived bioconcentration factors (BCF) in fish in the range of 15 to 60 L/kg wet.

In the terrestrial environment, category members are expected to exhibit a low order of toxicity based on calculated 14-day earthworm LC_{50} values ranging from 128 to 880 mg/kg soil.

TABLE OF CONTENTS

Tables

Figures

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Category

For purposes of the U.S. High Production Volume (HPV) Chemical Challenge Program (Program), the Alkyl Alcohols C6 - C13 Category test plan submitted in February 2003 (ExxonMobil Chemical Company, 2003) included seven Chemical Abstracts Service (CAS) registration numbers (RNs) (Table 1). The test plan identified existing data and additional data needed, based on an extensive technical review of the category, to adequately characterize the seven chemicals for the HPV Program endpoints. This category analysis report summarizes HPV Program data for the Alkyl Alcohols C6 - C13 Category, which contains seven CAS RNs.

Table 1. CAS RNs, and CAS RN Names in the Alkyl Alcohols C6 to C13 Category

CAS Numbers with TSCA Names:	68526-79-4	Hexanol, branched and linear
	70914-20-4	Alcohols C6-C8 branched
	68526-83-0	Alcohols C7-C9-iso, C8 rich*
	28473-21-4	Nonanol
	68526-84-1	Alcohols C8-C10-iso, C9 rich
	68526-85-2	Alcohols, C9-C11-iso, C10 rich
	68526-86-3	Alcohols C11-C14-iso, C13 rich
CAS Numbers with Molecular Formulas:	68526-79-4	C6H14O
	70914-20-4	C7H16O
	68526-83-0	C8H18O
	28473-21-4	C9H20O
	68526-84-1	C9H20O
	68526-85-2	C10H22O
	68526-86-3	C13H28O

* = Not currently HPV but included to facilitate category evaluation

Table 1 (Cont'd).

CAS Numbers with Structural Formulas:	68526-79-4	CH3-CH(CH3)-(CH2)3-OH (based on a C6 alcohol; general structure; contains various methyl branching patterns)
	70914-20-4	CH3-CH(CH3)-(CH2)4-OH (based on a C7 alcohol; general structure; contains various methyl branching patterns)
	68526-83-0	CH3-CH(CH3)-(CH2)5-OH (based on a C8 alcohol; general structure; contains various methyl branching patterns)
	28473-21-4	CH3-(CH2)8-OH
	68526-84-1	CH3-CH(CH3)-(CH2)6-OH (based on a C9 alcohol; general structure; contains essentially methyl branching patterns)
	68526-85-2	CH3-CH(CH3)-(CH2)7-OH (based on a C10 alcohol; general structure; contains various methyl branching patterns)
	68526-86-3	CH3-CH(CH3)-(CH2)10-OH (based on a C13 alcohol; general structure; contains various methyl branching patterns)
CAS Numbers with Molecular Weights:	68526-79-4	102.18
	70914-20-4	116.21
	68526-83-0	130.23
	28473-21-4	144.26
	68526-84-1	144.26
	68526-85-2	160.26
	68526-86-3	200.37
CAS Numbers with Synonyms:	68526-79-4	hexyl alcohol, isohexanol, Exxal 6
	70914-20-4	isoheptyl alcohol, isoheptanol, Exxal 7
	68526-83-0	isooctyl alcohol, isooctanol, Exxal 8
	28473-21-4	nonyl alcohol, nonan-1-ol
	68526-84-1	isononyl alcohol, isononanol, Exxal 9
	68526-85-2	isodecyl alcohol, isodecanol, Exxal 10
	68526-86-3	tridecyl alcohol, isotridecanol, Exxal 13

1.2 Purity/Impurities/Additives

Hexanol, branched and linear (CAS# 68526-79-4)

Commercial hexanol, branched and linear, is a clear, almost colourless liquid with a typical alcohol purity of 98%. The commercial product typically consists of three isomers with the following composition: 44 percent 1-hexanol, 53 percent methylpentanols, and 3 percent 2-ethylbutanol (Falbe, et al, 1984). Hexanol, branched and linear does not contain additives.

Alcohols C6-C8 branched (CAS# 70914-20-4)

Commercial Alcohols C6-C8 branched, is a clear, almost colourless liquid with a mild odor and a typical alcohol purity of 98%. The commercial product typically consists of methyl-1-hexanols. Alcohols C6-C8, branched does not contain additives.

Alcohols C7-C9-iso, C8 rich (CAS# 68526-83-0)

Commercial Alcohol C7-C9 iso, C8 rich, is a clear, almost colourless liquid with a typical alcohol purity of 99%. The commercial product typically consists of methyl-1-heptanols and/or dimethyl-1-hexanols; the composition and CAS registry number depend on the olefin feedstock. Alcohols C7-C9-iso, C8 rich does not contain additives.

Nonanol (CAS# 28473-21-4)

Commercial nonanol, is a clear, colourless liquid with a typical alcohol purity of >98%. The commercial product typically consists of approximately 80% 3,5,5-Trimethylhexanol. Nonanol does not contain additives.

Alcohols C8-C10-iso, C9 rich (CAS# 68526-84-1)

Commercial Alcohol C8-C10-iso, C9 rich is a clear, colourless liquid with a typical alcohol purity of 99.6%. The commercial product typically consists of primarily dimethyl-1-heptanols and methyl-1-octanols. The composition and CAS registry number depend on the olefin feedstock. Alcohols C8-C10-iso, C9 rich does not contain additives.

Alcohols C9-C11-iso, C10 rich (CAS# 68526-85-2)

Commercial Alcohols C9-C11-iso, C10 rich is a clear, colourless liquid with a typical alcohol purity of 99.6%. The commercial product typically consists of tri-methyl-1-heptanols and dimethyl-1-octanols. The composition and CAS registry number depend on the olefin feedstock. Alcohols C9-C11-iso, C10 rich does not contain additives.

Alcohols C11-C14-iso, C13 rich (CAS# 68526-86-3)

Commercial alcohol C11-C14-iso C13 rich is a clear, colourless liquid with a typical alcohol purity of 99.8%. A major isomer of a commercial-grade product is tetramethyl-1-nonanol. Alcohols C11-C14-iso, C13 rich does not contain additives.

Table 2 lists approximate carbon number distributions for members of the Alkyl Alcohols C6 to C13 Category.

Table 2. Approximate Carbon Number Distribution of Members in the Alkyl Alcohols C6 to C13 Category

Category Member	CAS Number	Composition (wt. %)
Hexanol, branched and linear	68526-79-4	C6 >95% Low levels of C7, C8
Alcohols, C6-C8-branched	70914-20-4	C7 >83% C6, C8 >4 to 17%
Alcohols, C7-C9-iso, C8-rich	68526-83-0	C8 >90% Low levels of C7, C9
Nonanol	28473-21-4	C9 approximately 100%
Alcohols, C8-C10-iso, C9-rich	68526-84-1	C9 >70% C10 >25% Low levels of C8
Alcohols, C9-C11-iso, C10-rich	68526-85-2	C10 >85% C9, C11 >4 to 7%
Alcohols, C11-C14-iso, C13-rich	68526-86-3	C12, C13 combined 90% Low levels of C11, C14

1.3 Physico-Chemical Properties

Category members have comparable structure and physical-chemical, environmental, and toxicological properties. Table 1 presents a summary of the physical-chemical properties exhibited by category members.

Table 3. Selected Physical Properties of Alkyl Alcohols C6 - C13

CAS NUMBER	Chemical Name	Boiling Range (º C)	Melting Point (º C)	Vapor Pressure (hPa @ 25ºC)	Relative Density (g/cm^3)	Log K_{ow}	Water Solubility (mg/L @ 25ºC)
68526-79-4	Hexanol, branched and linear	152 - 163	-49.3 [a]	2.56 [c]	0.827	1.8 - 2.0[a]	10,340 - 11,950[a]
70914-20-4	Alcohols C6-C8, branched	167 - 176 (152 [c])	-37.2 [a]	0.58 [a]	0.827	1.8 - 2.6[a]	3,539 - 11,950[a]
68526-83-0	Alcohols C7-C9-iso, C8 rich*	185 - 193 (213 [c])	-65	2.59 [c]	0.831	2.9 - 3.4[b]	1,379 - 1,485[a]
28473-21-4	Nonanol	192 - 204 (206 [c])	-18.65 [a]	0.40[a]	0.832	3.2 - 4.9[b]	128[b]
68526-84-1	Alcohols C8-C10-iso, C9 rich	202 - 219	-54	0.054[a]	0.832	3.8 - 4.3[b]	90.4[a]
68526-85-2	Alcohols C9-C11-iso, C10 rich	216 - 226	-40	0.018[a]	0.837	4.2 - 4.3[b]	75.0[b]
68526-86-3	Alcohols C11-C14-iso, C13 rich	250 - 270	<-40	0.002[a]	0.846	4.8 - 5.5[b]	5.8[b]

* = Not currently HPV but included to facilitate category evaluation

[a] Calculated using EPIWIN
[b] Measured values (Robust summaries are attached)(EMBSI, 1998; Letinski, *et.al*, 2002)
[c] Experimental values supplied by EPIWIN experimental database.

1.4 Category Justification

The Alkyl Alcohols C6 to C13 Category is a family of saturated alcohols that are produced from olefins by the hydroformylation or "oxo" process. Hydroformylation is the reaction of an olefin with carbon monoxide and hydrogen to produce an aldehyde, and its subsequent hydrogenation to the alcohol. The number of carbon atoms in the category members ranges from 6 to 13. Category members contain predominantly branched alkyl groups. Each substance consists of an isomeric mixture of saturated primary alcohols of high purity, and the following basic structure: CH_3-R-CH_2-OH, where R is a branched isomeric structure.

Table 4 shows a general structure for each Category member as well as the analogue substances (grey-shaded cells), which are not included in the Category, but which have similar structure and properties of sufficient similarity to be of value in supporting selected endpoints of the Category members. The analogues are not produced by ExxonMobil and therefore not included in this category.

Table 4. General Structure for Category Members and Analogue Substances.

CAS RN	IUPAC Name	R Length (C number)	Structure of R	In Category
111-27-3	1-Hexanol	C5	Linear	No *
111-87-5	1-Octanol	C8	Linear	No *
143-08-8	1-Nonanol	C9	Linear	No *
112-30-1	1-Decanol	C10	Linear	No *
112-53-8	1-Dodecanol	C12	Linear	No *
68526-79-4	Hexanol, branched and linear	C4	Branched**	Yes
70914-20-4	Alcohols, C6-C8-branched	C5	Branched**	Yes
68526-83-0	Alcohols, C7-C9-iso, C8-rich	C6	Branched**	Yes
28473-21-4	Nonanol	C7	Branched**	Yes
68526-84-1	Alcohols C8-C10-iso, C9 rich	C7	Branched**	Yes
68526-85-2	Alcohols C9-C11-iso, C10 rich	C8	Branched**	Yes
68526-86-3	Alcohols C11-C14-iso, C13 rich	C11	Branched**	Yes

* analogue substance used for supporting information ** primarily methyl branched (isomeric structures)

The justification for the Alkyl Alcohols C6 to C13 Category is that the members have:

- similar chemical structures,
- similar physico-chemical properties,
- comparable environmental fate,
- the same mode of action.

In general, aliphatic alcohol toxicity occurs by non-polar narcosis (Lipnick *et al.*, 1985). The mode of action is disruption of biological membrane function (van Wezel and Opperhuizen, 1995). Metabolic pathways, through which alcohols are metabolized, are likely to include similar reactions for all category members and result in structurally similar metabolites (carboxylic acids).

The data demonstrate that the category is valid for a screening-level hazard assessment for the Category and its members. One can assess the untested endpoints by extrapolation between and among the category members.

2 GENERAL INFORMATION ON EXPOSURE

Alkyl Alcohols C6 to C13 Category substances are used as chemical intermediates and applications of these can include co-solvents, anti-foaming agents, solvent extraction and flotation. Exposure to substances in the Alkyl Alcohols C6 to C13 Category may occur at workplaces where they are manufactured. Based on physical properties, the primary workplace exposure would be through inhalation and dermal contact. Alkyl Alcohols C6 to C13 are handled in industrial manufacturing and processing facilities and the majority of the applications involve incorporation of the alcohols into a matrix. Therefore, minimal consumer exposure is foreseen, since the consumer is only indirectly exposed through the use of the applications and uptake is expected to be low.

At production sites, potential exposure to Alkyl Alcohols C6 to C13 in the environment is low because there are no direct releases to the environment and process, storage, and handling facilities are enclosed. Based on the physico-chemical properties of category members, Alkyl Alcohols C6 to C13 at equilibrium in the environment will partition mainly to water (C6 to C10) with a shift to the sediment compartment as carbon chain length increases (C13).

2.1 Production Volumes and Use Pattern

Hexanol, branched and linear (CAS# 68526-79-4)

Isohexyl alcohol is made in the oxo process by reaction of pentenes with carbon monoxide and hydrogen in the presence of a catalyst, followed by hydrogenation (Falbe, et al, 1984). A major use of isohexyl alcohol is as a chemical intermediate in the production of esters, such as phthalates and acetates (Clayton and Clayton, 1994).

Alcohols C6-C8 branched (CAS# 70914-20-4)

Isoheptyl alcohol is made in the oxo process by reaction of hexenes with carbon monoxide and hydrogen in the presence of a catalyst, followed by hydrogenation (Falbe, et al, 1984). A major use of isoheptyl alcohol is as a chemical intermediate in the production of ester compounds, such as phthalate plasticizers and esters of carboxylic acids (Clayton and Clayton, 1994). Isoheptyl alcohols are also used as solvents or solubilizers in paint and printing inks, as a component in textile auxiliaries and

pesticides, for hormone extraction and in the surfactant field as foam boosters or antifrothing agents (Falbe, et al, 1984).

Alcohols C7-C9-iso, C8 rich (CAS# 68526-83-0)

Isooctyl alcohols are a mixture of isomeric C8 alcohols that are made by the oxo process by reaction of heptenes with carbon monoxide and hydrogen in the presence of a catalyst, followed by hydrogenation (Falbe, et al, 1984). The principle use of these alcohols is in the preparation of plasticizers, mainly dioctyl phthalate, but also esters of adipic, sebacic, azelmic, and trimellitic acids (Falbe, et al, 1984). Isooctyl alcohol is also used as a solvent for fats, oils, and waxes, as well as various rubber formulations and resins (Clayton and Clayton, 1994).

Nonanol (CAS# 28473-21-4)

1-Nonanol is produced by the high-pressure catalytic reduction of esters of pelargonic acid (Clayton and Clayton, 1994). A major use of 1-nonanol is as a chemical intermediate in the production of esters, and in fragrances (Clayton and Clayton, 1994).

Alcohols C8-C10-iso, C9 rich (CAS# 68526-84-1)

Isononyl alcohol is made in the oxo process by reacting olefins with carbon monoxide and hydrogen in the presence of a catalyst, followed by hydrogenation (Falbe *et al.,* 1984). A major use of isononyl alcohol is as a chemical intermediate in the production of esters, such as phthalates, acetates, and adipates. Isononyl alcohol is frequently used in the paint industry (Clayton and Clayton, 1994).

Alcohols C9-C11-iso, C10 rich (CAS# 68526-85-2)

Isodecyl alcohol or the C10 oxo alcohols are made in the oxo process by reacting nonenes with carbon monoxide and hydrogen in the presence of a catalyst, followed by hydrogenation (Falbe *et al.,* 1984). A major use of this alcohol is in the production of plasticizers (Clayton and Clayton, 1994).

Alcohols C11-C14-iso, C13 rich (CAS# 68526-86-3)

Isotridecyl alcohol is produced by the oxo process in which dodecenes are reacted with carbon monoxide and hydrogen in the presence of a catalyst, followed by hydrogenation (Falbe *et al.,* 1984). These alcohols are used in the production of plasticizers because of their low volatility. They are also used as a surfactant raw material, as a lubricant intermediate, and as a solvent (Falbe *et al.,* 1984).

2.2 Environmental Exposure and Fate

There is no information on environmental concentrations for substances in the Alkyl Alcohols C6 to C13 Category.

2.2.1 Sources of Environmental Exposure

Alkyl Alcohols C6 to C13 Category substances are used as chemical intermediates and additional applications of these can include co-solvents, anti-foaming agents, solvent extraction and flotation. Essentially, Alkyl Alcohols C6 to C13 released during manufacture enter the wastewater treatment facility (WWTF) where they can be biodegraded rapidly or sorbed to sewage sludge, which is either incinerated or landfilled (personal communication EMBSI, 2005a). The latter severely hinders their further migration because alkyl alcohols have a low potential to migrate through soil as suggested by

their K_{oc} values. Henry's Law Constant, a measure of the potential of a molecule to evaporate from open water, indicates that the molecules comprising category members will not volatilize at an appreciable rate, if released to water. However, once in air, these molecules would be subject to rapid atmospheric degradation via hydroxyl radical attack with calculated half-lives of less than 24 hours. Process, storage, and handling operations are conducted in enclosed facilities. Over-spills are collected and treated (via WWTF), and air from production plants and pumping stations is collected and incinerated.

2.2.2 Photodegradation

In air, a chemical can react with photosensitised oxygen in the form of $^{\bullet}OH$ or ozone (O_3). These reactions can result in a degradative change in the parent chemical that can ultimately lead to its complete degradation. Substances in the Alkyl Alcohols C6 to C13 Category can rapidly react with $^{\bullet}OH$ in air, which can be a predominant daylight atmospheric degradation process for this chemical. They can also react with O_3.

Potential $^{\bullet}OH$ reaction rate and atmospheric chemical half-life is calculated based on an average $^{\bullet}OH$ radical concentration. The atmospheric oxidation potential model (EPIWIN, 1999; Meylan and Howard, 1993) calculates a rate constant for the Alkyl Alcohols C6 to C13 Category members ranging from 21.3E-12 to 10.0E-12 $cm^3mol^{-1}s^{-1}$ and an average atmospheric half-life ranging from 6.0 to 12.9 hours or 0.50 to 1.1 days, respectively. These values are based on a 12-hour day (the 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated). The rate constants were calculated using an average global $^{\bullet}OH$ concentration of 1.5E6 $^{\bullet}OH/cm^3$. Because the $^{\bullet}OH$ radical is produced photolytically, the $^{\bullet}OH$ radical is present at significant concentrations only during daylight hours, and its concentration exhibits a marked diurnal profile, with a maximum concentration at around solar noon (depending on cloud cover) and with low or negligible concentrations at night (Boethling and Mackay, 2000).

These data indicate that indirect photodegradation of Alkyl Alcohols C6 to C13 Category substances can occur at a rapid rate, however, based on their low vapor pressure it is not expected to contribute significantly to their degradation in the environment.

Direct photochemical degradation in aqueous solution occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. A prerequisite for direct photodegradation is the ability of one or more bonds within a chemical to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer.

An approach to assessing the potential for a substance to undergo photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by constituent molecules (Zepp and Cline, 1977). Substances in the Alkyl Alcohols C6 to C13 Category contain molecules that are oxygenated aliphatic compounds which will absorb only in the far UV region, below 220 nm, (Boethling and Mackay, 2000) and therefore will not undergo direct photolysis. These data indicate that photolysis will not significantly contribute to the degradation of alkyl alcohols in the aquatic environment.

2.2.3 Stability in Water

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond, thereby changing the parent chemical. Chemicals that are susceptible to hydrolysis contain functional groups that can be displaced by a nucleophilic substitution reaction. Potentially hydrolyzable groups include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris, 1982). The lack of a suitable leaving group renders a compound resistant to hydrolysis. Alkyl Alcohols C6 to C13 are resistant to hydrolysis because they lack a functional group that is hydrolytically reactive (Harris, 1982). Therefore, hydrolysis will not contribute to their removal from the environment.

2.2.4 Transport between Environmental Compartments

Henry's Law Constants (HLCs) representing potential volatility from water were calculated for chemicals within this category (Table 5). The HLCs for the Category members range from 0.02 to 45.1 $Pa \cdot m^3$/mole. There is no formal scheme to classify Henry's constant, but these data suggest that category members would not volatilise from water at appreciable rates.

Table 5. Calculated Henry's Law Constants

CAS NUMBER	Chemical Name	Henry's Law Constant ($Pa\text{-}m^3$/mole)
68526-79-4	Hexanol, branched and linear	2.19
70914-20-4	Alcohols C6-C8, branched	0.02
68526-83-0	Alcohols C7-C9-iso, C8 rich	0.25
28473-21-4	Nonanol	45.1
68526-84-1	Alcohols C8-C10-iso, C9 rich	8.62
68526-85-2	Alcohols C9-C11-iso, C10 rich	3.80
68526-86-3	Alcohols C11-C14-iso, C13 rich	6.91

Fugacity-based multimedia modelling provides basic information on the relative distribution of a chemical between selected environmental compartments (i.e., air, soil, water, and sediment). Fugacity is a physical chemistry concept and can be regarded as the "escaping tendency" of a chemical from a phase (environmental compartment).

The Mackay model requires the input of basic physicochemical parameters such as molecular weight, melting point, vapor pressure, water solubility, log K_{ow} (as found in Table 3). As stated previously, the Alkyl Alcohols C6 to C13 are primarily manufacturing intermediates. As such, discharge of these products is expected to be primarily to water. Mackay Level III modeling (Mackay *et al.,* 1996; Mackay, 2003) was performed assuming 100% discharge to water. Default half-lives for degradability needed to run the model were used as per the EU Technical Guidance Document on the Use of Multimedia Models for Estimating Overall Environmental Persistance and Long-range Transport (OECD, 2004). Default half-lives were as follows: readily biodegradable (water = 5 days; soil = 30 d); pass test, but fail 10-d window (water = 10 d; soil = 90 d). Half-lives for sediment were 10 times that

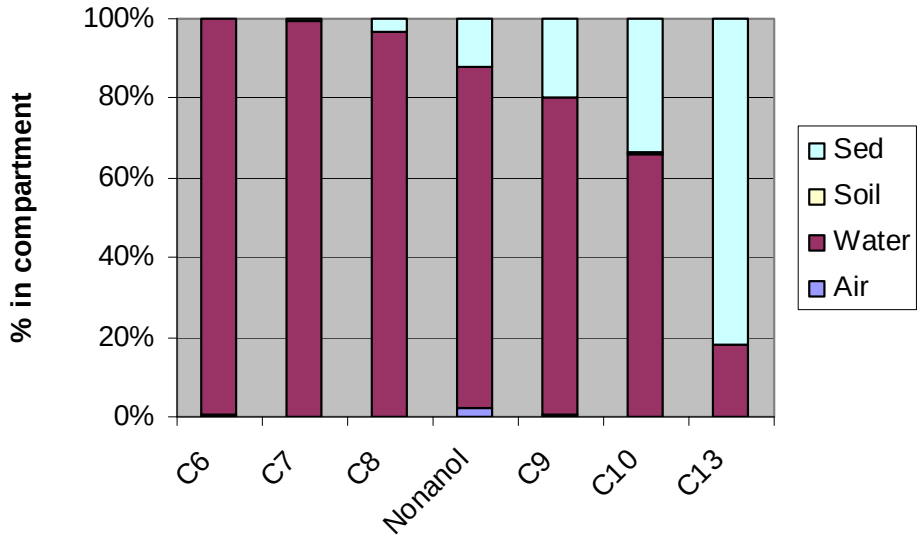
in soil. Half-lives for air were based on Atmospheric Oxidation Potential as calculated by AOPWIN version 1.89 (EPIWIN, 1999; Meylan and Howard, 1993).

Results of the Mackay Level III environmental distribution model (Table 6) suggest a high environmental distribution into the water compartment for alcohols with a carbon chain length of C6 to C10. The model also predicts a high environmental distribution into the sediment compartment for alcohols C11-C14-iso, C13 rich. To illustrate the distribution trend, results of the Level III modelling, based on carbon number, are also depicted in Figure 1.

Table 6. Environmental distribution as calculated by the Mackay (2003) Level III fugacity model.

Substance (CAS RN)	Environmental Distribution (%) per Compartment			
	Air	Water	Soil	Sediment
Hexanol, branched and linear (68526-79-4)	0.3	99.4	0.02	0.2
Alcohols C6-C8, branched (70914-20-4)	<0.01	99.4	0.02	0.5
Alcohols C7-C9-iso, C8 rich (68526-83-0)	0.03	96.6	0.03	3.3
Nonanol (28473-21-4)	2.1	86.0	0.05	11.9
Alcohols C8-10-iso, C9 rich (68526-84-1)	0.8	79.5	0.03	19.7
Alcohols C9-C11-iso, C10 rich (68526-85-2)	0.2	66.0	0.03	33.8
Alcohols C11-14-iso, C13 rich (68526-86-3)	0.08	18.3	0.01	81.6

Figure 1: Select results of Fugacity Modeling using the Mackay Level III Model



2.2.5 Biodegradation

Aerobic

Substances in this category have the potential to biodegrade in aerobic systems (from 60% to greater than 84% of biodegradation within 28 days, in ready biodegradability tests), and they are either readily or inherently biodegradable. The inherently biodegradable materials, although exceeding the criteria of 60% biodegradation in 28 days, did not do so within the 10-day window necessary for a "readily biodegradable" designation.

The manometric test procedure uses continuously stirred, closed systems, with a non-acclimated inoculum obtained from a domestic wastewater treatment plant. Percent biodegradation is based on oxygen consumption or carbon dioxide (CO_2) evolution. The continual stirring applied in these test systems is recommended when assessing the biodegradability of low to moderately water-soluble substances like those in this category.

Hexanol, branched and linear (CAS# 68526-79-4)

Alcohols C6-C8 branched (CAS# 70914-20-4)

No data are available.

Alcohols C7-C9-iso, C8 rich (CAS# 68526-83-0)

In a manometric respirometry (OECD 301F) study, using non-acclimated inocula (domestic activated sludge), Alcohols C7-C9-iso, C8 rich was shown to biodegrade 82% in 28 days (EMBSI, 1996a). The results of the study are based on O_2 consumption and the theoretical oxygen demand of the test chemical as calculated using results of an elemental analysis of the test chemical. This material was considered "readily biodegradable" under the conditions of the study.

Nonanol (CAS# 28473-21-4)

In another manometric respirometry (OECD 301F) study, using non-acclimated inocula (domestic activated sludge), nonanol was shown to biodegrade 84% in 28 days (EMBSI, 1998a). The results of the study are based on O_2 consumption and the theoretical oxygen demand of the test chemical as calculated using results of an elemental analysis of the test chemical. This material was considered "readily biodegradable" under the conditions of the study.

Alcohols C8-C10-iso, C9 rich (CAS# 68526-84-1)

No data are available.

Alcohols C9-C11-iso, C10 rich (CAS# 68526-85-2)

In a manometric respirometry (OECD 301F) study, using non-acclimated inocula (domestic activated sludge), Alcohols C9-C11-iso, C10 rich was shown to biodegrade 71% in 28 days (EMBSI, 1997a). The results of the study are based on O_2 consumption and the theoretical oxygen demand of the test chemical as calculated using results of an elemental analysis of the test chemical. This material was considered "inherently biodegradable" under the conditions of the study.

Alcohols C11-C14-iso, C13 rich (CAS# 68526-86-3)

Biodegradability of Alcohols C11-C14-iso, C13 rich was examined following procedures outlined in OECD test guidelines (OECD 301F). In this manometric respirometry study, using non-acclimated inocula (domestic activated sludge), Alcohols C11-C14-iso, C13 rich was shown to biodegrade 60.6% in 28 days (EMBSI, 2003a). In two additional studies with the same C13 alcohol (CAS RN 68526-85-2), following the same study procedures, results of 58% and 59.6% biodegradation in 28 days were reported (EMBSI, 1998b, 1997b). The results of all three studies are based on O_2 consumption and the theoretical oxygen demand of the test chemical as calculated using results of an elemental analysis of the test chemical. This material was considered "inherently biodegradable" under the conditions of the studies.

Anaerobic

No data are available.

2.2.6 Bioaccumulation

Members of the Alkyl Alcohols C6 to C13 Category are characterized by log K_{ow} values in the range of 1.8 to 5.5. These moderate to high log K_{ow} values suggest a potential bioconcentration concern, particularly for Category members with a carbon chain length of C9 or greater.

Biochemical evidence for alcohol biotransformation was reviewed by de Wolf and Parkerton (1999), and strongly suggests that alcohol bioconcentration is much likely lower than predicted by simple log K_{ow} correlation. This is primarily because higher alcohols are readily metabolized by alcohol and aldehyde dehydrogenases to the corresponding carboxylic acid. The biotransformation of alcohols to carboxylic acids is a biochemical process which is ubiquitous in the plant and animal kingdom (de

Wolf and Parkerton, 1999), and has been specifically identified in a number of aquatic and terrestrial species.

The results of bioconcentration testing in rainbow trout (*Oncorhynchus mykiss*) clearly show the lack of bioconcentration of the alcohols tested, and category members are expected to exhibit a low potential to bioaccumulate based on measured bioconcentration (BCF) data. Two aqueous bioconcentration studies (OECD TG 305) were conducted using C10 (CAS RN 68526-85-2) and C13 (CAS RN 68526-86-3) alcohols (EMBSI, 1998c; 1999a). In the studies, rainbow trout were exposed to aqueous concentrations of the category members for periods of 16 and 10 days, respectively, followed by depuration periods of 10 and 4 days, respectively. The C10 alcohol resulted in a BCF value ranging from 14.8 to 15.5 L/kg wet (mean of 15.2 L/kg wet) and the C13 alcohol resulted in a BCF ranging from 30 to 60 L/kg wet (mean of 45 L/kg wet).

The above data along with the biochemical evidence discussed suggest that the Alkyl Alcohols C6 to C13 Category members have a low potential for bioconcentration in aquatic species and are not expected to bioaccumulate.

2.2.7 Other Information on Environmental Fate

Using the EPIWIN v.3.12 estimation program, members of the Alkyl Alcohols C6 to C13 Category are expected to be removed from wastewater treatment facilities >95%. The predominant mechanism accounting for removal in a wastewater treatment facility is biodegradation, followed by partitioning of the alcohol to sludge, which in Europe is incinerated and in the United States is either incinerated or landfilled (personal communication EMBSI, 2005a).

2.3 Human Exposure

2.3.1 Occupational Exposure

Limited workplace exposure data are available for members of the Alkyl Alcohol C6 to C13 Category. Exposure to these alcohols can occur through inhalation (primary route) and dermal contact (Clayton and Clayton, 1994). Potential for worker exposure exists during manufacturing line maintenance, turnarounds, sample collection, and tank and barge loading. Limited air sampling data suggest that concentrations are well below 50 ppm (EMBSI, 1998d) for an 8-hour TWA. This level equates to approximately 209, 238, 266, 299, 323, and 409 mg/m^3 for C6, C7, C8, C9, C10, and C13 alcohols, respectively (ExxonMobil, 2001a, 2003a-e). Personnel exposures in manufacturing facilities are low because the process, storage, and handling operations are enclosed.

2.3.2 Consumer Exposure

Alkyl Alcohols C6 to C13 are handled in industrial manufacturing and processing facilities and the majority of the applications involve incorporation of the alcohols into a matrix. Therefore, minimal consumer exposure is foreseen, since the consumer is only indirectly exposed through the use of the applications and uptake is expected to be low.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Alkyl Alcohols C6 to C13 would likely be broken down by mitochondrial beta-oxidation or by cytochrome P450-mediated ω- and ω-1-oxidation (may be followed by β-oxidation). The alcohol undergoes various oxidative steps to yield other alcohols, ketones, aldehydes, carboxylic acids and carbon dioxide (Mann, 1987). Data for monohydric, saturated alcohols show a systematic variation according to molecular weight in a manner similar to many other homologous series (Monick, 1968). The analogs 1-hexanol and 1-dodecanol follow similar metabolic pathways by undergoing oxidative steps to yield aldehydes, carboxylic acid and eventually undergoing intermediary metabolism (van Beilen *et al*., 1992). The body handles aliphatic hydrocarbons in a similar manner via oxidative conversion to alcohols, ketones, and eventual elimination as carbon dioxide and carboxylic acids (Wislocki *et al.*, 1980). The undegraded alcohols can be conjugated either directly or as a metabolite with glucuronic acid, sulfuric acid, or glycine and are rapidly excreted (Lington and Bevan, 1994). Glucuronidation and glutathione conjugation are possible means of rapid elimination (Mann, 1987).

Studies in Animals

No pharmacokinetic studies have been conducted with any members of the Alkyl Alcohols C6 to C13 Category.

Studies in Humans

No pharmacokinetic studies have been conducted with any members of the Alkyl Alcohols C6 to C13 Category in humans.

3.1.2 Acute Toxicity

Studies in Animals

Oral

Hexanol, branched and linear (CAS 68526-79-4)

A homologous series of branched primary alcohols was tested for its acute oral toxicity in a comparative study. Groups of five male rats each received a single dose by gavage, were observed for 7–14 days and subjected to gross pathology. The investigation of hexanol (CAS 68526-79-4) resulted in an LD_{50} of 3670 mg/kg (Scala and Burtis, 1973; Hazleton, 1960).

Alcohols C6-C8, branched (CAS 70914-20-4)

A toxicity study was conducted on Alcohols C6-C8, branched (CAS 70914-20-4) at oral doses of 1000, 1470, 2150, 3160, 4640, 6810 or 10000 mg/kg. Groups of five male rats each received a single dose by gavage. The rats were observed for 7–14 days and subjected to gross pathology. Signs of toxicity included respiratory rate decreases, fecal staining, decreased motor

activity and hypothermia. All five animals at the 6810 and 10000 mg/kg dose levels died. Two animals died at the 4640 mg/kg level, and one animal each died at the 1000, 2150 and 3160 mg/kg dose levels. There were no deaths at the 1470 mg/kg dose level. The resultant LD_{50} was calculated as 3900 mg/kg (Esso, 1979).

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

An oral toxicity study was conducted on Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0) in five male and female rats by gavage at the limit dose of 2000 mg/kg. Observations were recorded for 14 days and consisted of sedation, ventral body position in males, hunched posture, and ruffled fur. However, all animals had recovered within 6 days of dosing. At necropsy, no macroscopic abnormalities were observed. The LD_{50} was >2000 mg/kg (RCC, 1988a).

Nonanol (CAS 28473-21-4)

No data are available.

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

In a toxicity study with male rats conducted on Alcohols, C8-10-iso, C9 rich (CAS 68526-84-1), no deaths occurred during the 14-day observation period at levels of 34.6, 120, 417, and 1450 mg/kg after administration of a single dose by oral gavage (Esso, 1968a; Scala and Burtis, 1973). Two of the five animals at the 5000 mg/kg dose level, and all five animals at the 10,000 mg/kg dose level died within 24 hours. Depression, labored respiration and evidence of excessive urination and/or diarrhea were observed at the two highest dose levels within one hour of administration. At necropsy, abscessed or dark red lungs, and a dark zone between the renal cortex and medulla were observed in animals from the 5000 and 10,000 mg/kg dose levels. The acute oral LD_{50} value was 2970 mg/kg.

Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2)

An acute oral toxicity study was conducted in male rats with Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2). Animals were administered a single dose by oral gavage at levels of 26, 82, 260, 820, 2600, and 8200 mg/kg (Esso, 1960a). All five animals in the 8200 mg/kg dose group died within the first four hours of the seven-day observation period. No other mortality was observed. Clinical signs of toxicity included a dose-response for oily fur, inactivity, labored breathing, ataxia, lacrimation, and limb splaying. Survivors generally appeared normal within 24-48 hours. Gross necropsies performed on animals from the 8200 mg/kg dose group revealed congested lungs, kidneys, and adrenals, and dark-appearing spleens. No abnormalities were observed in animals from the other dose groups. Normal weight gain was observed in the surviving animals. The calculated LD_{50} value for Alcohols, C9-C11-iso, C10 rich was 4626 mg/kg.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

A study was conducted on Alcohols, C11-C14-iso, C13 rich (CAS 68526-86-3) using male and female rats (RCC, 1988b). The animals were gavaged with a single dose at a level of 2000 mg/kg followed by a 14-day observation period. No deaths occurred in either sex producing an LD_{50} value greater than 2000 mg/kg. Clinical signs of toxicity observed included sedation, diarrhea, and dyspnea (males). There were no macroscopic changes observed at necropsy.

Dermal

Hexanol, branched and linear (CAS 68526-79-4)

A single dermal application of Hexanol, branched and linear (CAS 68526-79-4) was made to four groups of four rabbits at doses of 82, 259, 820, and 2600 mg/kg to the abraded abdominal skin under occlusive dressing. There were no mortalities at any dosage level tested. The LD_{50} in albino rabbits is greater than the highest dose tested (approximately 2600 mg/kg body weight). Observations for signs of toxicity were made at one, four, and 24 hours after compound administration and daily thereafter for a total of seven days. Signs of toxicity included labored respiration and central nervous system depression. All animals recovered within 4-48 hours after the exposure period began. Moderate erythema and edema were observed. The LD_{50} was greater than 2600 mg/kg (Hazleton Laboratories, 1960; Scala and Burtis, 1973)

Alcohols C6-C8, branched (CAS 70914-20-4)

A dermal toxicity study of Alcohols C6-C8, branched (CAS 70914-20-4) was conducted in male and female rabbits at 50, 200, 794 and 3,160 mg/kg. A single dermal application was made to abraded abdominal skin under occlusive dressing. Observations were recorded at one, two, and four hours after dosing, and daily thereafter for a total of 14 days. No deaths occurred in the study resulting in a LD_{50} greater than 3160 mg/kg (Exxon Research and Engineering, 1979a).

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

A dermal toxicity study of Alcohols C7-C9, branched (CAS 68526-83-0) was conducted in male and female rabbits at 83, 262, 820, and 2623 mg/kg. At the highest dose (2623 mg/kg), animals exhibited labored respiration and were inactive. One animal in the high dose group died within 24 hours. The remaining animals in this dose group returned to normal appearance and behavior 2 days after the treatment. All other animals in the study exhibited no signs of toxicity. The LD_{50} for the study was greater than 2623 mg/kg, (Hazleton Laboratories, 1960; Scala and Burtis, 1973).

Nonanol (CAS 28473-21-4)

No data are available.

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

Scala and Burtis (1973) reported dermal LD_{50} values in rabbits of >3160 mg/kg for alcohol C8-C10 iso, C9 rich (CAS 68526-84-1). The animals were given a single application of the test substance to abraded abdominal skin under occlusive dressing. No deaths were reported during the 14-day observation period.

Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2)

Scala and Burtis (1973) reported a dermal LD_{50} in rabbits >2600 mg/kg for Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2). The animals were administered a single application of the test substance at 80, 260, 820, or 2600 mg/kg to abraded abdominal skin under occlusive dressing. No deaths were reported and no gross pathological findings were observed at necropsy, (Scala and Burtis, 1973; Esso, 1960b).

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

Scala and Burtis (1973) reported a dermal LD_{50} value in rabbits of >2600 mg/kg for alcohol C11-C14 iso, C13 rich. The animals were given a single application of the test substance to abraded abdominal skin under occlusive dressing. No deaths were reported.

Inhalation

Hexanol, branched and linear (CAS 68526-79-4)

Hexyl alcohol was administered to rats, mice, and guinea pigs for 6-hours at a saturated vapor concentration of 1060 ppm followed by a 14-day observation period. No mortality was observed in any species providing an LC_{50} value greater than 1060 ppm (Scala and Burtis, 1973). However, the animals showed moderate irritation of the upper respiratory tract, slight congestion of the lungs, and signs of slight CNS depression (Clayton and Clayton, 1994). All signs of systemic effects cleared soon after termination of exposure.

Alcohols C6-C8, branched (CAS 70914-20-4)

No deaths or treatment-related effects were reported in rats, mice, or guinea pigs exposed to iosheptanol vapor at a concentration of 152 ppm (0.72 mg/l calculated) for 6 hours (Clayton and Clayton, 1994). The LC_{50} for all three species was greater than 152 ppm.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

Isooctyl and 2-ethylhexyl alcohols were administered to rats, mice, and guinea pigs for 6-hours at asaturated vapor concentrations of 200 and 227 ppm, respectively, followed by a 14-day observation period. No mortality was observed in any species resulting in a LC_{50} value greater than 200 ppm for the isooctyl alcohol and greater than 227 ppm for 2-ethylhexyl alcohol (Scala and Burtis, 1973).

Nonanol (CAS 28473-21-4)

No data are available.

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

Isononyl alcohol was administered to rats, mice and guinea pigs for 6 hours at a nominal vapor concentration of 3630 ppm (approximately 21.7 mg/l) followed by a 14-day observation period. There were no deaths during the exposure, but 2/10 rats and 1/10 mice died during the first 14-hours post exposure. No guinea pigs died during the study. Systemic effects related to central nervous system depression were seen that included inactivity, shallow, or labored respiration and prostration. Local irritation effects were seen, but quickly returned to normal at the termination of exposure. The LC_{50} values for all species were greater than 3630 ppm nominal concentration (Esso, 1968b; Scala and Burtis, 1973).

Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2)

Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2) were administered to rats, mice and guinea pigs for 6 hours at a nominal vapor concentration of 95 ppm (approximately 0.6 mg/l) followed by a 14-day

observation period. No mortality was observed in any species providing an LC_{50} value greater than 95 ppm nominal concentration (Esso, 1960b; Scala and Burtis, 1973).

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

Tridecyl alcohol (CAS 68526-86-3) was administered to rats, mice, and guinea pigs for 6-hours at a nominal vapor concentration of 12 ppm (0.1 mg/l calculated) followed by a 14-day observation period. No mortality was observed in any species providing an LC_{50} value greater than 12 ppm nominal concentration (Scala and Burtis, 1973).

Conclusion

Members of the Alkyl Alcohols C6 to C13 Category have a low order of acute toxicity by the oral, dermal, and inhalation routes of exposure.

3.1.3 Irritation

Skin Irritation

Hexanol, branched and linear (CAS 68526-79-4)

A study conducted with a single 24-hour application of hexanol, branched and linear (CAS 68526-79-4) to intact rabbit skin produced moderate irritation (Hazleton Laboratories, 1960; Scala and Burtis, 1973). Skin irritation consisted of slight to moderate erythema, moderate edema, atonia, and desquamation. Erythema, atonia, and desquamation gradually diminished in intensity, but persisted to termination on Day 14.

Alcohols C6-C8, branched (CAS 70914-20-4)

A study conducted with a single 24-hour application of Alcohols C6-C8, branched (CAS 70914-20-4) to intact rabbit skin produced significant irritation (Exxon Research and Engineering, 1979a). Group mean scores at 24, 48, and 72 hours were 1.5, 2.0, 4.0 for erythema and 2.5, 2.5, and 2.5 for edema. Dermal reactions were seen in all animals from Day 7 to 14.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

Alcohols C7-C9-iso, C8 rich produced moderate irritation to intact rabbit skin when applied for 4 and 24 hours. A single 4-hour application resulted in a primary irritation index of 3.08. Mean scores at 24, 48, and 72-hours were 1.83, 1.83, and 2.0 for erythema and 0.83, 1.33, and 1.5 for edema (Hazleton Laboratories, 1960; Scala and Burtis, 1973).

Nonanol (CAS 28473-21-4)

No data are available.

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

A study conducted with a single 24-hour application of Alcohols, C8 to C10-iso, C9 rich (CAS 68526-84-1) to intact rabbit skin produced marked irritation (Esso, 1968c; Scala and Burtis, 1973). Skin irritation consisted of slight to severe erythema, slight to moderate edema and atonia, and slight to severe desquamation. Erythema disappeared by the eleventh day, edema by the fourth day, while desquamation persisted to termination on Day 14.

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2), produced moderate irritation to intact rabbit skin when applied for 4 hours (EMBSI, 1992). Six New Zealand white rabbits were used in the study. A single 4-hour application of 0.5 ml undiluted test substance under semi-occlusive conditions resulted in a Primary Irritation Index (PII) of 2.16 (on a scale of 0-8) (moderate irritant). The mean scores at 24, 48, and 72 hours were 1.33, 1.33 and 1.83, respectively for erythema and 0.33, 0.5 and 0.83, respectively for edema.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

Alcohols, C11 to C14-iso, C13 rich (CAS 68526-86-3), produced mild to moderate irritation to intact rabbit skin when applied for 4 hours. A single 4-hour application of 0.5 ml undiluted test substance under semi-occluded test conditions resulted in a Primary Irritation Index (PII) of 2.4 (on a scale of 0-8) (moderate irritant). The mean scores at 24, 48, and 72 hours were 2.0, 2.0 and 2.0, respectively for erythema and 0.33, 0 and 0, respectively for edema (RCC, 1989).

In another study, the same C13 alcohol resulted in a Primary Irritation Index (PII) of 1.8 (on a scale of 0-8) (mild irritant). A single 4-hour application of 0.5 ml undiluted test substance under semi-occluded test conditions was used on 3 male and 3 female New Zealand White rabbits. The mean scores at 24, 48, and 72 hours were 1.33, 1.0 and 1.0, respectively for erythema and 1.17, 0.5 and 0.17, respectively for edema (Safepharm, 1993a).

Eye Irritation

Hexanol, branched and linear (CAS 68526-79-4)

Hexyl alcohol was evaluated for eye irritation in rabbits. Hexyl alcohol was administered in a single application to the left eye of each of six rabbits (Scala and Burtis, 1973; Clayton and Clayton, 1994). The untreated eye served as the control. Hexyl alcohol caused severe eye irritation involving all eye structures and was based on persistent iritis, corneal opacity, and in two animals, corneal vascularization.

Alcohols C6-C8, branched (CAS 70914-20-4)

Alcohols C6-C8, branched produced severe irritation in the eyes of rabbits. In one study, conjunctival irritation generally cleared by 10 days (Exxon Research and Engineering, 1979b). Group maximum Draize scores (out of a possible 110) were: 24 at 24 hours; 28 at 72 hours; and 5 at 7 days. The maximum total Draize score observed was 51. Group means scores at 24, 48, and 72 hours for the various indices were: 1.5, 1.5, 1.33 for conjunctival redness; 2.17, 2.5, 2 for chemosis; 1.0, 0.83, 0.83 for iridial irritation; 1.33, 1.5, 1.17 for corneal opacity.

In another study (BioDynamics, 1980), Alcohols C6-C8, branched, produced severe irritation with a maximum Draize score of 46 at 24 hours after exposure. Mean scores at 24, 48, and 72 hours were 2.0, 2.0 and 1.83, respectively for conjunctival redness; 2.0, 1.33 and 1.33 for chemosis; 1.0, 0.83 and 0.67, for iridial effects; and 2.0, 1.67 and 1.67, for corneal opacity.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

Isooctyl and 2-ethylhexyl alcohols produced significant irritation in the eyes of rabbits (Scala and Burtis, 1973). Both materials produced persistent, widespread corneal opacity which generally cleared within 7 days. Median scores for acute eye irritation at 24, and 72 hours, and at 7 days were 26, 18, and 0 for isooctyl alcohol, and 19, 20, and 0 for 2-ethylhexanol, respectively.

Nonanol (CAS 28473-21-4)

No data are available.

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

Eye irritation studies have been conducted on C9 alcohols and Alcohols C8 to C10-iso, C9 rich (CAS 68526-84-1). In one study, the C9 alcohol produced severe irritation in the eyes of rabbits that generally cleared in 10 days (Esso, 1968c; Scala and Burtis, 1973). The alcohol was rated a marked irritant. Mean scores at 24, 48, and 72 hours were 3.0, 2.83 and 2.0, respectively for conjunctival redness; 1.33, 0.17 and 0, respectively for chemosis; 1, 0.83 and 0.17, respectively for iridial effects; and 1.17, 1.0 and 0.83, respectively for corneal opacity. The maximum Draize score for the study was 33 (out of a possible 110), which was recorded at 72 hours after exposure.

In another study (Safepharm, 1993b), Alcohols, C8 to C10-iso, C9 rich, produced moderate irritation with a maximum Draize score of 23.2 at 24 hours after exposure. Mean scores at 24, 48, and 72 hours were 1.8, 1.3 and 1.2, respectively for conjunctival redness; 1.3, 1.2 and 0.67 respectively for chemosis; 0.83, 0.67 and 0.33, respectively for iridial effects; and 0.83, 0.83 and 0.83, respectively for corneal opacity. Irritation had generally cleared by Day 7.

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

Alcohols, C9 to C11-iso, C10 rich (CAS 68526-85-2), produced significant conjunctival irritation in the eyes of rabbits which generally cleared in 7 days (Esso, 1970; Scala and Burtis, 1973). The C10 alcohol was rated as a severe eye irritant due to corneal sloughing or pitting. The mean scores at 24, 48, and 72 hours were 1.8, 1.5 and 1.3, respectively for conjunctival redness; 0.5, 0 and 0, respectively for chemosis; 0.67, 0.5, 0.33, respectively for iridial irritation; and 0.5, 0.5 and 0.33, respectively for corneal opacity. The maximum Draize score for the study was 28 (out of 110) and was recorded at 24 hours after exposure.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

Alcohols, C11 to C14-iso, C13 rich (CAS 68526-86-3) produced moderate irritation in the unrinsed eyes of rabbits which generally cleared by 7 days (RCC, 1988b). Mean scores at 24, 48, and 72 hours were 1.7, 1.3 and 0.7, respectively for conjunctival redness; and 0.7, 0.3 and 0, respectively for

chemosis; 0, 0.7 and 0.3, respectively for iridial irritation; and 1.0, 1.0 and 1.0, respectively for corneal opacity. Ocular discharge was observed in all rabbits during the first 72 hours, with clearing by Day 7. No staining of the cornea or conjunctivae was observed in the rabbits during the study that could be related to the test substance.

Respiratory Tract Irritation

Hexanol, branched and linear (CAS 68526-79-4)

Alcohols C6-C8, branched (CAS 70914-20-4)

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

Nonanol (CAS 28473-21-4)

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

No data are available

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

The upper airway sensory irritation potential of Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2) was evaluated in male Swiss Webster mice using ASTM E981-84 (EMBSI, 1993). Four male mice per group received head-only exposures for 30 minutes to the test substance generated as a vapor at 111 and 168 ppm (maximum achievable). Respiratory rates were monitored before, during and after exposure, to establish a baseline respiratory rate, and to evaluate the animals' sensory irritation response to the test atmosphere. There were no deaths during the exposure, or during the post-exposure period. There was no evidence of pulmonary irritation (deep lung) and none of the animals in either group showed ocular abnormalities during or after the exposure. Breathing patterns characteristic of moderate upper airway sensory irritation were observed in both groups (111 and 168 ppm). The vapor concentration of 111 ppm resulted in 32% decrease in breathing rate and the concentration of 168 ppm resulted in 40% decrease in breathing rate. Neither of the respiratory rate decreases exceeded 50%, therefore an RD_{50} concentration could only be estimated. The calculated RD_{50} was 280 ppm.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

No data are available.

3.1.4 Sensitization

Dermal

No skin sensitization studies have been conducted**.** However, a sensitization study using a structurally similar C6 chemical, 1-hexanol (CAS 111-27-3), showed no indication of sensitization in guinea pigs using the Magnusson-Kligman procedure (Clayton and Clayton, 1994).

Studies in Humans

No skin sensitization studies have been conducted with members of the Alkyl Alcohols C6 to C13 Category on humans. However, based on negative human data on a structurally similar C6 chemical, 1-hexanol (CAS 111-27-3) (Clayton and Clayton, 1994), category members are not likely to be skin sensitizers.

Respiratory Tract

Studies in Animals

No data are available.

Studies in Humans

No respiratory tract sensitization studies have been conducted with members of the Alkyl Alcohols C6 to C13 Category in humans. However, due to the low vapor pressure of members of this category, atmospheric exposure is expected to be low at ambient temperatures.

3.1.5 Repeated Dose Toxicity Studies in Animals

Studies in Animals

Inhalation

A repeated dose inhalation study was reported for nonyl alcohol (Egorev et al, 1964). Rabbits were exposed to concentrations of 0.2; 0.6 and 0.8 mg/l (33, 99 and 136 ppm) for 2 h/day for 2 months. Small amounts of deformed or degenerate glial elements diffusely scattered in the cerebal cortex and subcortex were observed. No other effects were reported. Although details on the study design and results in this older study were not available, it can be used in a weight of evidence evaluation.

Oral

An evaluation of the available repeated dose studies indicates that Alkyl Alcohols C6 - C13 have a low order of subchronic toxicity. Additionally, summaries of the subchronic studies with the analog substances 1-hexanol (CAS 111-27-3), 2-ethylhexanol, and 1-dodecanol are publicly available from the European Chemicals Bureau (ECB) IUCLID database and are included with this submission (ECB, 2000a,b).

Hexanol, branched and linear (CAS 68526-79-4)

Subchronic toxicity data on 1-hexanol (CAS 111-27-3), an isomer of Alkyl Alcohol C6, indicates that this material has a low order of subchronic toxicity. Thirteen-week dietary feeding studies in both the rat and dog produced a NOAEL greater than or equal to 0.5% in the diet, (ECB, 2000a).

Alcohols C6-C8, branched (CAS 70914-20-4)

In a two-week oral study, male rats were dosed with 1 mmol/kg (130 mg/kg) of iso-octanol (Rhodes, *et al*., 1984). After acclimation for 1 week, five animals received 1mmol/kg/day (130 mg/kg/day) of the test substance by oral gavage and ten animals received only the vehicle, PEG 300, daily for 14 days. Animals were sacrificed after 14 days and blood was analysed for plasma cholesterol and triglycerides. The liver was removed for histopathological analysis, analysis of catalase, and CN-insensitive palmitoyl CoA oxidation. Testicular weight was also determined. Polyethylene glycol 300 served as a solvent control and was administered to ten rats in parallel. Iso-octanol did not significantly change bodyweight gain, liver to bodyweight ratio, or testis to bodyweight ratio when compared to the solvent control. There was a slight induction of palmitoyl CoA oxidase activity. However, the activity of other peroxisome-associated enzymes was not affected and overall peroxisome number was not effected. The rats did not develop testicular atrophy, liver enlargement, hepatic peroxisome induction, or hyperlipidemia. Under the conditions of the study, iso-octanol has a low order of repeated dose toxicity to male rats for the endpoints studied. The NOAEL was the limit dose of 130 mg/kg.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

A number of studies have evaluated the toxicity of repeated exposure to 2-ethylhexanol, an isomer of Alkyl Alcohol C7-9. In a 3-month study in rats, 2-ethylhexanol was administered by oral gavage at doses of 25, 125, 250, and 500 mg/kg/day. At the highest doses (250 and 500 mg/kg/day), changes in body and organ weights were observed. Increased liver weights (relative to body weight) were observed in both sexes at 250 and 500 mg/kg/day. Increased stomach weights (relative to body weight) were also observed in both sexes at 500 mg/kg/day and in the females only at 250 mg/kg/day. There were no substance related changes in the kidneys, brain, adrenal glands, ovaries or testes (relative to body weight) at any of the dose levels. No other effects were observed in gross or histological examinations which could be related to the test substance administration. The NOEL for the study was 125 mg/kg/day and the LOEL for the study was 250 mg/kg/day based on body weight changes (BASF, 1991).

Dermal exposure of rats to 0.4 and 2.0 g/kg/day hexyl alcohol or Alkyl Alcohol C7 - 9, branched for 10 days resulted in no clinical signs of toxicity at any time during the study. All animals survived to study termination and there were no treatment-related clinical, in-life, gross postmortem or microscopic findings. The no observable adverse effect level (NOAEL) for repeat dermal exposure was 2.0 g/kg/day, (Esso, 1961).

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

In a two-week oral study, five male rats were dosed orally (gavage) with 144 mg/kg/day (1 mmol/kg/day) of isononanol (Rhodes *et al*., 1984) following a 1 week acclimation. In the control group, ten animals received the vehicle, PEG (polyethylene glycol) 300, daily for 14 days. Animals were sacrificed after 14 days and blood was analyzed for plasma cholesterol and triglycerides. The liver was removed for histopathological analysis, analysis of catalase, and CN-insensitive palmitoyl CoA oxidation. Testicular weight was also determined. Isononanol did not significantly influence

bodyweight gain, liver to bodyweight ratio, or testis to bodyweight ratio when compared to the control group. However, there was a slight induction of palmitoyl CoA oxidase activity, but the activity of other peroxisome-associated enzymes was not affected and overall peroxisome number was not effected. The rats did not develop testicular atrophy, liver enlargement, hepatic peroxisome induction, or hyperlipidemia. The NOAEL was set at the limit dose of 144 mg/kg/day.

In another study with nonyl alcohol (CAS RN unspecified) (Treon, 1962), rabbits were given repeated oral doses of 148 mg/kg bw/day over a 83-day period, once per day, five days per week. The animals exhibited normal growth patterns throughout the course of the study. No mortality was observed, and there were no signs of intoxication.

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

A comparative screening study to selectively investigate the effect on testis and liver morphology and function was conducted with the analog isodecanol, (CAS RN 25339-17-7) (Rhodes *et al*., 1984). After acclimation for 1 week, five male rats received 168 mg/kg/day (1 mmol/kg/day) of the test substance by oral gavage. In the control group, ten animals received the vehicle, PEG (polyethylene glycol) 300, daily for 14 days. Animals were sacrificed after 14 days and blood was analyzed for plasma cholesterol and triglycerides. The liver was removed for histopathological analysis, analysis of catalase, and CN-insensitive palmitoyl CoA oxidation. No significant effects were observed on relative liver weight, relative testes weight, serum lipids, or peroxisomal liver enzymes. The NOAEL was set at the limit dose of 168 mg/kg/day.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

A study was performed with an analog substance, 1-dodecanol (CAS RN 112-53-8), using the Combined Repeat Dose and Reproductive/ Developmental Toxicity Screening Test protocol (Hansen, 1992). Male and female rats were administered 1-dodecanol orally via the feed at doses of 100, 500, and 2000 mg/kg/day for a period of 14 days. 1-Dodecanol at doses up to 2000 mg/kg/day had no influence on body weight, weight gain, food consumption and reproductive efficiency in the parental generation. No organ toxicity was observed in the females.

A comparative 14-day *screening* study to investigate selectively the effect on testis and liver morphology and function was conducted with tridecanol (CAS RN 27458-92-0) (Rhodes *et al.,* 1984). After acclimation for 1 week, five male rats received 184 mg/kg/day (1 mmol/kg/day) of the test substance by oral gavage. In the control group, ten animals received the solvent, PEG (polyethylene glycol) 300, daily for 14 days. Animals were sacrificed after 14 days and blood was analysed for plasma cholesterol and triglycerides. The liver was removed for histopathological analysis, analysis of catalase, and CN-insensitive palmitoyl CoA oxidation. No significant effects were observed on relative liver weight, relative testes weight, serum lipids, or peroxisomal liver enzymes. The NOAEL was set at the limit dose of 184 mg/kg/day.

Conclusion

Taken together, the results of these studies demonstrate that Alkyl Alcohols C6-C13 have a low order or toxicity under conditions of repeat exposure by both the oral and dermal routes. In addition, they demonstrate that the members of the category display a consistent degree of subchronic toxicity by either the oral or dermal routes of exposure. Therefore, Alkyl Alcohols C6-C13 do not require further testing to assess subchronic toxicity.

3.1.6 Mutagenicity

In vitro Studies

Hexanol, branched and linear (CAS 68526-79-4)

Data on 1-hexanol (CAS 111-27-3), which is an isomer of hexanol, branched and linear, indicates that this material is not genotoxic (ECB, 2000a). Two studies using *Salmonella typhimurium,* with and without metabolic activation, were negative for mutagenicity. Both studies followed OECD TG 471 with concentrations of 8, 40, 200, 1000, and 5000 µg/plate in the first study, and concentrations of 6.25, 25, 100, 400, and 1600 µg/plate in the second study.

Alcohols C6-C8, branched (CAS 70914-20-4)

Alcohols C6-C8, branched was evaluated for the potential to induce structural chromosomal aberrations in cultured Chinese Hamster Ovary (CHO) cells (EMBSI, 2005b). The study was conducted in two phases; an initial chromosomal aberration assay with a 19-hour harvest time, and a repeat assay with both 19 and 43-hour cell harvest times. Both phases were conducted with (+S9) and without (-S9) metabolic activation. There were no statistically significant differences or dose-related trends noted at any dose level in the initial or repeat assay. Alcohols, C6-C8, branched did not induce chromosomal aberrations in CHO cells in the initial or repeat assay.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

2-ethyl-1-hexanol (CAS 104-76-7), an isomer of alcohols C7-C9-iso, C8 rich, was evaluated using the Ames Assay in the presence and absence of metabolic activation. Using five strains of *Salmonella typhimurium,* the material was not mutagenic (Shimizu *et al.,* 1985). Test concentrations were 1, 5, 10, 50, 100, 500, and 1000 µg/plate. All samples were run in duplicate.

Nonanol (CAS 28473-21-4)

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

No data are available.

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

The analog substance, isodecanol (CAS RN 25339-17-7), was tested in a chromosomal aberration assay according to OECD Test Method 473 (Fraunhofer Institute, 1993). V79 Chinese hamster lung fibroblasts were used in the cytogenetic assay at concentrations of 5 to 20 µg/ml with and without metabolic activation. Following exposure, the cells were treated with colcemid (to arrest cells in metaphase), harvested and chromosome preparations were made. The preparations were stained with Giemsa and metaphase cells were analyzed for chromosomal aberrations. Cytotoxicity measured as the depression of the mitotic index was previously examined. The cytotoxic concentration was 20 µg/ml and was chosen as the maximum dose for testing. Each 100-cell spread metaphases per treatment group were examined and two independent experiments were performed. Using ethanol as the solvent, the following tests were conducted: a) without S-9 mix, fixation time 21 hr after start of treatment at concentrations of 5, 10 and 20 µg/ml; b) with S-9 mix, exposure 3 hr, fixation time 18 hr after start of treatment at concentrations of 5, 10 and 20 µg/ml; c) with S-9 mix, exposure 3 hr, fixation time 21 hr after start of treatment at concentrations of 5, 10 and 20 µg/ml. The positive controls substances were

ethylmethane-sulfonate (500 µg/ml) and cyclophosphamide (5 µg/ml). Under the conditions of the assay, isodecanol did not induce chromosomal aberrations in cultured mammalian V79 cells with or without metabolic activation.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

A study was conducted with an analog substance, 1-dodecanol (CAS RN 112-53-8), using *Salmonella typhimurium* strains TA98, 100, 1535, 1537, and 1538 at concentrations of 0.01, 0.05, 0.1, 0.5, 1, 5, 10 and 50 µg/plate (Shimizu *et al.,* 1985), following procedures similar to those of the OECD TG 471. 1-dodecanol (90% pure) was dissolved in DMSO at appropriate concentrations. 0.1ml of this mixture was added to 0.1 ml of bacteria and 0.5 ml of either S9 mix (polychlorinated biphenyl-induced rat liver S9 mixture) or phosphate-buffered saline. Following a 20-minute pre-incubation, the mixtures were combined with agar and incubated for 48 hours. Colonies were scored with an automatic counter. All tests were performed in duplicate. 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (AF-2), N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG), 9-aminoacridine (9AC), 4-nitroquinoline-1-oxide (4NQO), benzo(a)pyrene (B(a)P), 2-amino-anthracene (2AA), and 2-nitrofluorene (2NF) were used as positive controls. The study showed no evidence of mutagenic activity with and without metabolic activation.

A second study conducted with the analog substance 1-dodecanol (CAS RN 112-53-8) using *Escherichia coli* (WP2uvrA) also found the test substance to exhibit no mutagenic activity at concentrations of 0.01, 0.05, 0.1, 0.5, 1, 5, 10 and 50 µg/plate with and without metabolic activation (Shimizu *et al.,* 1985). The study was performed following procedures, similar to those of the OECD TG 471. 1-dodecanol (90% pure) was dissolved in DMSO at appropriate concentrations. 0.1ml of the mixture was added to 0.1 ml of bacteria and 0.5 ml of either S9 mix (polychlorinated biphenyl-induced rat liver S9 mixture) or phosphate-buffered saline. Following a 20-minute pre-incubation, the mixtures were combined with agar and incubated for 48 hours. Colonies were scored with an automatic counter. All tests were performed in duplicate. 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide (AF-2), N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG), 9-aminoacridine (9AC), 4-nitroquinoline-1-oxide (4NQO), benzo(a)pyrene (B(a)P), 2-aminoanthracene (2AA), and 2-nitrofluorene (2NF) were used as positive controls.

In vivo Studies

Hexanol, branched and linear (CAS 68526-79-4)

Alcohols C6-C8, branched (CAS 70914-20-4)

No data are available.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

In reports cited by the US EPA, the analogue substance 2-ethyl-1-hexanol (CAS 104-76-7), produced negative results in both a mouse micronucleus test and a rat cytogenetic assay (ECB, 2000b). The mice were exposed to a single i.p. injection at a dose of 456 mg/kg, a level equal to 80% of the 7-day LD_{50}. Bone marrow was harvested 30 hours post application and 1000 PCE/animal were scored for the presence of micronuclei. Male rats in the cytogenetic assay were exposed via oral gavage for 5 days to doses of 0.02, 0.07, and 0.21 ml/kg/day. Of the 50 metaphase bone marrow cells examined from each animal, no significant increase in chromatid and chromosome breaks or structural rearrangements were noted.

Nonanol (CAS 28473-21-4)

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

Barylak and Kosaschuk (1988) reported a cytogenetic assay with nonyl alcohol (CAS RN unspecified). Rats received a 40% suspension in water at dose levels of 2.26 to 12.8 mg/kg by gavage. Fifty bone marrow cells were examined for each animal approximately 48 hours after dosing. Only 3 % of the cells were observed with aberrations, which was not considered statistically significant from the controls. However, only limited details of the study were available but no mutagenic effects were reported.

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

In a cytogenetic assay, isodecyl alcohol (CAS RN 25339-17-7) was administered orally to rats as a 40% suspension in water at dose levels of 2.26 to 12.8 mg/kg (Barylak and Kosaschuk, 1988). Fifty bone marrow cells were examined for each animal approximately 48 hours after dosing. Only 3.4% of the cells were observed with aberrations, which was not considered statistically significant. Limited details of the study were available but no mutagenic effects were reported.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

A mouse micronucleus assay was carried out with the analog substance 1-dodecanol (CAS RN 112-53-8) (Banduhn, 1992). Albino CFW-1 mice were administered 1-dodecanol orally at a dose of 5000 mg/kg with exposure periods of 24, 48, and 72 hours. The study was performed following test procedures outlined in OECD TG 474. No statistically significant enhanced mean values of micronucleated cells in polychromatic erythrocytes were observed. There was also no reduction in the ratio of polychromatic to normochromatic erythrocytes.

Conclusion

Although mutagenicity studies have not been carried out on the specific Category members, studies have been carried out on a number analog substances that are major components of the members. Studies have been conducted in accordance with OECD test guideline 471, employing *Salmonella typhimurium* as well as *Escherichia coli* and have not given any indications of genotoxic effects, either with or without metabolic activation. In another *in vitro* test, a chromosomal aberration assay using V79 Chinese hamster lung fibroblasts, no mutagenic effects were found with and without metabolic activation. Additionally, *in vivo* bone marrow micronucleus assays conducted in mice and rats showed no mutagenic effects. Based on the findings of these studies, the members of the Alkyl Alcohols C6-C13 Category are not expected to exhibit mutagenic activity with or without metabolic activation. Thus, the mutagenic potential for the Alkyl Alcohols C6-C13 Category has been well characterized and no further studies are proposed.

Further data to support the hazard assessment for the category comes from a similar series of Alkyl Acetates C6-C13. These materials have also been shown to be non-genotoxic in the Ames assay (EMBSI, 1995a; 1994a,b). Alkyl acetates are manufactured from the alkyl alcohols and undergo metabolism by esterases to produce acetic acid and the corresponding alkyl alcohol. As indicated in a previous test plan submitted for the alkyl acetates, there is no evidence for genotoxicity with these compounds in a variety of strains of *S. typhimurium* in the presence or absence of metabolic activation. The C6, C6-C8, C7-C9, and C11-C14 alkyl acetates, all of which are metabolized to the corresponding alkyl alcohol, produced negative results in the Ames test. These data, in conjunction with the negative data on structural isomers of these materials provide strong evidence that Alkyl Alcohols C6-C13 are not genotoxic.

3.1.7 Carcinogenicity

Conclusion

No chronic toxicity or carcinogenicity studies have been conducted on Alkyl Alcohols C6 to C13 Category members. Two studies, one with rats and the other with mice, were conducted using 2-ethyl-1-hexanol (CAS 104-76-7). The test substance was not oncogenic in either study (ECB, 2000b). Based on the negative genotoxicity data reported previously, along with the two studies using the analogue substance 2-ethyl-1-hexanol, members of the Alkyl Alcohol C6 to C13 Category are expected to have a low potential for carcinogenicity.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

Hexanol, branched and linear (CAS 68526-79-4)

Alcohols C6-C8, branched (CAS 70914-20-4)

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

No data are available.

Alcohols C8-C10-iso, C9 rich (CAS RN 68526-84-1)

A comparative screening study to selectively investigate the effects on the testis and liver was conducted with isononanol (Rhodes *et al*., 1984). After acclimation for 1 week, five male rats received 144 mg/kg/day (1 mmol/kg/day) of the test substance by oral gavage. No significant effects were found for relative testes weight or morphology (testicular atrophy). The NOAEL was set at the limit dose of 144 mg/kg/day.

Alcohols C9-C11-iso, C10 rich (CAS RN 68526-85-2)

A comparative screening study to selectively investigate the effect on testis and liver was conducted with the analog substance isodecanol (CAS RN 25339-17-7) (Rhodes *et al*., 1984). After acclimation for 1 week, five male rats received 168 mg/kg/day (1 mmol/kg/day) of the test substance by oral gavage. No significant effects were found for relative testes weight or morphology (testicular atrophy). The NOAEL was set at the limit dose of 168 mg/kg/day.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

No data are available.

Developmental Toxicity

Hexanol, branched and linear (CAS 68526-79-4)

The analog 1-hexanol was tested in a rat developmental toxicity study by the inhalation route of exposure (Nelson, *et al.*, 1989). Fifteen Sprague-Dawley females were exposed to vapor concentrations of 3500 mg/m^3 for 7 hours/day during gestation days 1-19. Sham controls were exposed to room air. Throughout the study, all animals were housed under standard environmental conditions and allowed free access to food and water except when the pregnant females were in the exposure chamber. Dams were weighed daily for the first week of exposure and weekly thereafter. Exposures were conducted in Hinners-type chambers. The purity of the test substance was >99% as measured by gas chromatography. On Day 20, dams were sacrificed and the uterus and ovaries were removed and examined for corpa lutea, implantations, resorption sites, and live fetuses. Fetuses were removed and examined for external malformations, sexed, weighed, and examined for visceral or skeletal defects.

No treatment-related effects were observed in dams. There were no significant fetal malformations associated with inhalation of 1-hexanol by the dam. There was a slight but statistically significant increase in resorptions (1.3 versus 0.4 per litter for controls). However, this resorption mean was still in the range seen in historical controls. Under the conditions of this study, inhalation of saturated vapor atmospheres of 1-hexanol was not maternally toxic or teratogenic in rats. Thus, the Maternal and Fetal NOAEL was 3500 mg/m^3.

Alcohols C6-C8, branched (CAS 70914-20-4)

No data are available.

Alcohols C7-C9-iso, C8 rich (CAS 68526-83-0)

Alcohols C7-C9-iso, C8 rich was examined for its effects on prenatal developmental toxicity according to OECD Guideline 414, by administering a test substance solution in corn oil to 25 mated female Wistar rats/group by oral gavage at doses of 100, 500 and 1000 mg/kg body weight on Day 6 through Day 15 of gestation. A standard dose volume of 5 ml/kg body weight was used for each group. The control group, consisting of 25 females, was dosed with the vehicle only (corn oil). Food consumption and body weight were recorded regularly through out the study period. The state of health was checked daily. All surviving dams were sacrificed on gestation Day 21 and assessed by gross pathology (including weights of unopened uterus and the placenta). All live fetuses were weighed, sexed externally, and examined externally for gross malformations. Approximately one-half of the fetuses were prepared for examination of abnormalities of the head. The viscera of all these fetuses were immediately examined by dissection. The remaining half of the live fetuses was preserved for examination of skeletal abnormalities.

Adverse clinical signs were observed in 8 of the 24 dams in the high dose group (1000 mg/kg-bw/day). These signs included emaciation, decreased food consumption, abdominal/anogenital staining, rales, hypoactivity, and little or no stool. The symptoms were transient and generally were not observed following cessation of dosing. The remaining dams in the high dose group had incidental findings such as alopecia, but otherwise appeared normal throughout the study. There were no observable abnormalities in dams of the middle and low dose groups throughout the gestational period. There were no maternal findings at necropsy that were judged to be the result of treatment with the test substance. For the most part, uterine implantation parameters were equivalent between the treated and control groups.

There were slight differences between the high dose group (1000 mg/kg-bw/day) and the control group in the number of post-implantation losses and resorptions, however these differences were not statistically significant and were deemed to be due to the poor health of the dams.

Mean fetal body weight was equivalent between treated and control fetuses of both sexes. Three low dose (100 mg/kg-bw/day), two mid dose (500 mg/kg-bw/day), and one high dose fetus were stunted. There were no statistically significant differences in mean skeletal ossification sites and in total or individual external, visceral, or skeletal malformations between control and treated groups. There were statistically significant increases in total fetuses with skeletal variations and in the incidence of hypoplastic skull bones in the high dose group when compared to controls. These findings were slightly higher than the historical control range of the lab and were not observed with litter-based analysis. Statistically significant increases in the number of lumbar ribs were observed in the middle and high dose groups. However, due to the lack of embryotoxicity observed in this study, these findings were attributed to maternal toxicity observed during treatment.

The no observed adverse effect level (NOAEL) for maternal toxicity was 500 mg/kg bw/day. The NOAEL for prenatal developmental toxicity was 1000 mg/kg bw/day. Under the conditions of the study, Alcohols, C7-C9-iso, C8 rich induces maternal toxicity at concentrations that are not embryotoxic (EMBSI, 1994c).

In another study, the analog substance 1-octanol was tested in a rat developmental toxicity study by the inhalation route of exposure (Nelson, *et al*., 1990). Fifteen Sprague-Dawley females were exposed to vapor concentrations of 400 mg/m^3 for 7 hours/day during gestation days 1-19. Sham controls were exposed to room air. Throughout the study, all animals were housed under standard environmental conditions and allowed free access to food and water except when the pregnant females were in the exposure chamber. Dams were weighed daily for the first week of exposure and weekly thereafter. Exposures were conducted in Hinners-type chambers. The purity of the test substance was 99% as measured by gas chromatography. On Day 20, dams were sacrificed and the uterus and ovaries were removed and examined for corpa lutea, implantations, resorption sites, and live fetuses. Fetuses were removed and examined for external malformations, sexed, weighed, and examined for visceral or skeletal defects.

No treatment-related effects were observed in dams. There were no statistically significant differences in maternal weight gain, feed consumption, or water intake between the control and treated groups. In addition, no signs of fetal toxicity were observed. There were no statistically significant differences between the mean number of corpora lutea and resorptions, the sex ratio, and the mean fetal weights between the control and treated groups. Under the conditions of this study, exposure of pregnant rats to 1-nonanol did not induce maternal or fetal toxicity. Thus, the Maternal and Fetal NOAEL was ≥400 mg/m^3.

Alcohols C8-C10-iso, C9 rich (CAS RN 68526-84-1)

Comparative screening studies of the analog substances isononyl alcohol 1 and 2 on the potential to induce prenatal developmental toxicity in rats were performed following requirements of OECD Guideline 414 with the exception that only 10 pregnant rats per group were used. Isononyl alcohol 1 consisted of isomers with a moderate degree of branching (dimethyl heptanols) and contained approximately 16% isodecanol. Isononyl alcohol 2 consisted of isomers with a low degree of branching (dimethyl heptanols and methyl octanols). Each test substance was administered by oral gavage at 144, 720 and 1440 mg/kg bw on gestation Days 6-15. Due to mortality in the high dose group, a supplementary study was conducted at 1080 mg/kg bw. Groups of 10 Wistar females per dose

level received the test or control substance at a standard dose volume of 5 ml/kg. Control group 1 was dosed with doubly distilled water. Control group 2 was dosed with emulsifier (doubly distilled water with 0.005% Cremophor EL). The state of health of the animals was monitored daily and food consumption and body weights of the animals were recorded regularly. Females were sacrificed on gestation Day 20. Fetuses were removed and evaluated for sex, weight, and any external, soft tissue, or skeletal findings.

The administration of isononyl 1 at 1440 mg/kg bw was lethal for all 10 dams (7 found dead on gestation Days 9 - 11, three had to be sacrificed on gestation Days 9 and 10) with additionally severe clinical signs of toxicity. The dose of 1080 mg/kg bw (supplementary study) was lethal for one dam and caused severe maternal toxicity in form of clinically findings like abdominal position, unsteady gait and apathy and affected food consumption and body weight parameter (including body weight loss). The gravid uterus weight was reduced and the post-implantation loss was distinctly increased due to a marked increase in the resorption rate. At 720 mg/kg bw, effects on the dams consisted of unsteady gait, nasal discharge, initially reduced food consumption and effects on body weight parameters including retarded body weight gain during treatment. The 144 mg/kg bw dose level had no effect on the dams.

Due to the deaths of all dams at the 1440 mg/kg bw level, no fetal observations could be obtained. Embryo/fetotoxicity at1080 mg/kg bw (supplementary study) consisted of a statistically significant increase in malformations (mainly related to the heart), retardations and an increased incidence of fetuses with rudimentary cervical rib(s). At 720 mg/kg bw numerically reduced fetal body weights and an increased number of skeletal variations and retardations as well as an increase in the incidence of fetuses with hydroureter occurred. This increased incidence was still present at 144 mg/kg bw. However, the significance of this endpoint as an indicator of marginal developmental toxicity is questionable.

Finally, isononyl alcohol 1 did not alter gestational parameters at doses that were not maternally toxic. Thus, the NOAEL for maternal and embryo/fetal toxicity was 144 mg/kg/day bw for isononyl alcohol 1.

The administration of isononyl alcohol 2 was lethal for 3 dams at 1440 mg/kg bw (one found dead on gestation Day 9, two had to be sacrificed on gestation Days 8 and 10). Further marked effects consisted of impaired state of health including abdominal or lateral position, unsteady gait and apathy, reduced food consumption, and body weight losses. At 1080 mg/kg bw (supplementary study) clinical symptoms such as unsteady gait and apathy, reduced food consumption, affected body weight parameter including transient body weight loss were recorded. The gravid uterus weight was slightly reduced and the post-implantation loss was slightly increased due to an increase in the resorption rate. The dose of 720 mg/kg bw caused clinical signs consisting of unsteady gait, salivation and piloerection in some dams, an initially reduced food consumption and body weight gain, while 144 mg/kg bw had no effect on the maternal organism. Signs of embryo/fetotoxicity at 1440 mg/kg bw consisted of markedly reduced fetal weights and an increased number of fetuses with common variations and skeletal retardations. No statistical significant increase in malformation was noted but one out of 91 fetuses (in six litters) had absent external genitalia. The 1080 mg/kg bw dose level (supplementary study) led to an increased number of fetuses with malformations concerning mainly the thoracic vertebrae. At 720 mg/kg bw an elevated number of fetuses with hydroureter occurred, but 144 mg/kg bw revealed no indications for embryo/fetotoxicity.

It was concluded that isononyl alcohol 2, when administered by oral gavage under the conditions of this study showed indications of embryo/fetotoxicity only at doses that induced overt maternal toxicity. Isononyl alcohol 2 did not alter gestational parameters at doses that were not maternally toxic. Consequently, the NOAEL for maternal and embryo/fetotoxicity for isononyl alcohol 2 was 144 mg/kg bw, (U.S. EPA, 1989a, Hellwig and Jaeckh, 1997, TSCATS, 1991a).

In another study, the analog 1-nonanol was tested in a rat developmental toxicity study by the inhalation route of exposure (Nelson, *et al*., 1990). Fifteen Sprague-Dawley females were exposed to vapor concentrations of 150 mg/m^3 for 7 hours/day during gestation Days 1-19. Sham controls were exposed to room air. Throughout the study, all animals were housed under standard environmental conditions and allowed free access to food and water except when the pregnant females were in the exposure chamber. Dams were weighed daily for the first week of exposure and weekly thereafter. Exposures were conducted in Hinners-type chambers. The purity of the test substance was 99% as measured by gas chromatography. On Day 20, dams were sacrificed and the uterus and ovaries were removed and examined for corpa lutea, implantations, resorption sites, and live fetuses. Fetuses were removed and examined for external malformations, sexed, weighed, and examined for visceral or skeletal defects.

No treatment-related effects were observed in dams. There were no statistically significant differences in maternal weight gain, feed consumption, or water intake between the control and treated groups. In addition, no signs of fetal toxicity were observed. There were no statistically significant differences between the mean number of corpora lutea and resorptions, the sex ratio, and the mean fetal weights between the control and treated groups. Under the conditions of this study, exposure of pregnant rats to 1-nonanol did not induce maternal or fetal toxicity. Thus, the Maternal and Fetal NOAEL was 150 mg/m^3.

Alcohols, C9-C11-iso, C10 rich (CAS 68526-85-2)

No data are available.

Alcohols C11-C14-iso, C13 rich (CAS 68526-86-3)

A one-generation study in rats (Hansen, 1992) was performed with the analog substance 1-dodecanol (CAS RN 112-53-8) using the Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test protocol. Male and female rats were administered 1-dodecanol orally via the feed at doses of 100, 500 and 2000 mg/kg/day for a period of 14 days. No effects were seen on reproductive or developmental parameters up to doses of 2000 mg/kg/day. 1-Dodecanol at the dose administered had no influence on body weight, weight gain, food consumption and reproductive efficiency in the parental generation. Pregnancy rates were not statistically altered and there were no differences in the lengths of the gestation periods. No organ toxicity was observed in the females, and there was no effect on the number of pups per litter, weight, sex ratio, or mortality rate from Days 1 to 5 after birth.

Conclusion

Developmental toxicity studies conducted by the oral route on alcohols, C7-C9-iso, C8 rich and isononyl alcohols produced consistent results and demonstrated that these materials do not affect reproductive parameters. Although a slight increase in resorptions was observed in the studies, this

only occurred in the highest dose group(s) and in the presence of overt maternal toxicity. As supporting information, testing of 1-dodecanol in a combined repeated dose developmental /reproductive study showed no effects to parents or offspring. Furthermore, inhalation exposure to saturated vapors of the linear alcohols, 1-hexanol and 1-octanol, did not induce any statistically significant changes in reproductive parameters. In the subchronic studies of isononyl alcohol and isodecyl alcohol, no changes in testicular weight were observed. These data support the conclusion that members of the Alkyl Alcohol C6 to C13 Category are not selective reproductive toxicants. Thus, the reproductive toxicity for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

3.2 Assessment Summary for Human Health

Members of the Alkyl Alcohols C6 to C13 Category have a low order of toxicity by the oral, dermal, and inhalation routes of exposure. Oral LD_{50}s ranged from >2000-3900 mg/kg and dermal LD_{50}s ranged from >2600-3160 mg/kg. Inhalation exposure studies were generally conducted at the maximum attainable saturated vapor concentrations ranging from 3630 ppm for the lighter C9s alcohols to12 ppm for the heavier C13 alcohols. Animals generally showed no signs of toxicity other than reversible CNS depression when exposed at these maximally attainable vapor concentrations. Thus, acute toxicity for the Alkyl Alcohols C6 to C13 Category has been well characterized and no further studies are proposed.

Members of the Alkyl Alcohols C6 to C13 Category are mildly to markedly irritating to the skin and mildly to severely irritating to the eyes. Additionally, Alcohol C9-11-iso, C10 rich produced moderate upper airway sensory irritation in male mice exposed to vapor atmospheres ranging from 111 to 168 ppm. Thus, the skin, eye, and respiratory tract irritation potential for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

Members of the Alkyl Alcohols C6 to C13 Category are not expected to be skin sensitizers in animals or humans. A structurally similar chemical, 1-hexanol, did not induce sensitising reactions in guinea pigs or humans. Data were not available to assess the potential for respiratory tract sensitization in animals or humans, however, since they are not expected to be skin sensitizers, it is not expected that category members would cause respiratory sensitization. Additionally, due to the low vapor pressure of most members of this category, atmospheric exposure is expected to be low. Although limited data are available to characterize the sensitization potential for the Alkyl Alcohol C6 to C13 Category, the irritant properties of these chemicals make further testing a low priority and no further studies are proposed.

Category members are expected to have a low order of subchronic toxicity. In comparative screening studies designed to evaluate the liver and testes, repeated oral doses of iso-nonanol, iso-decanol, and tridecanol for 14-days produced minimal hepatotoxic effects and no testicular effects in rats. No Observable Adverse Effects Levels (NOAEL) for the three substances were 144, 168, and 184 mg/kg/day, respectively. In other studies, repeated oral and dermal dosing of nonyl alcohol, produced a low order of toxicity in rabbits. Additionally, a combined repeated dose and reproductive / developmental toxicity screening study was conducted for 14 days using 1-dodecanol in rats. No effects on target organs were reported at the highest dose of 2000 mg/kg/day. In developmental toxicity studies with repeated dosing, the primary effects were reported to be CNS depression at the higher dose levels. Based on the results of the repeated-dose studies conducted in animals, the

members of the Alkyl Alcohols C6 to C13 Category appear to have a low order of subchronic toxicity and no further studies are proposed.

Studies carried out in accordance with OECD test guideline 471, employing *Salmonella typhimurium* have not given any indications of genotoxic effects, either with or without metabolic activation. In another *in vitro test*, a chromosomal aberration assay using Chinese hamster ovary cells, no mutagenic effects were found with and without metabolic activation. Additionally, *in vivo* bone marrow micronucleus assays conducted in mice and rats showed no mutagenic effects. Based on the findings of these studies, the members of the Alkyl Alcohols C6-C13 Category showed no mutagenic activity with or without metabolic activation. Thus, the mutagenic potential for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

Developmental toxicity studies conducted by the oral route on alcohols, C7-C9-iso, C8 rich and isononyl alcohols produced consistent results and demonstrated that these materials do not affect reproductive parameters. Although a slight increase in resorptions was observed in the studies, this only occurred in the highest dose group(s) and in the presence of overt maternal toxicity. As supporting information, testing of 1-dodecanol in a combined repeated dose developmental /reproductive study showed no effects to parents or offspring. Furthermore, inhalation exposure to saturated vapors of the linear alcohols, 1-hexanol and 1-octanol, did not induce any statistically significant changes in reproductive parameters. In subchronic repeat-dose studies of isononyl alcohol and isodecyl alcohol, no changes in testicular weight were observed. These data support the conclusion that members of the Alkyl Alcohol C6 to C13 Category are not selective reproductive toxicants. Thus, the reproductive toxicity for the Alkyl Alcohol C6 to C13 Category has been well characterized and no further studies are proposed.

In conclusion, members of the Alkyl Alcohol C6 to C13 category have a low order of acute toxicity, are not expected to skin or respiratory sensitizers, but have shown irritant effects to the skin, eyes, and upper respiratory tract. Subchronic studies have also shown a low order of toxicity. Although some slight effects on the liver were seen at high doses, these are likely the result of peroxisome proliferation and thus, do not pose a risk to humans. Testing in a variety of genotoxicity assays has not shown any mutagenic activity with or without metabolic activation. Based on the negative genotoxicity data, category members are expected to have a low potential for carcinogenicity. Reproductive/ developmental testing has shown fetal effects in some studies, but only at doses that produced overt maternal toxicity. The data support the conclusion that members of the category are not selective reproductive toxicants. Thus, the toxicity of the Alkyl Alcohol C6 to C13 Category has been well characterized and no further testing is proposed.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute Toxicity Test Results

Hexanol, branched and linear (CAS 68526-79-4)

The acute toxicity of Hexanol, branched and linear was investigated with a freshwater fish (*Pimephales promelas*) following test procedures developed by the USEPA. The study was conducted under flow-

through conditions. A stock solution was prepared at a nominal concentration of 3720 mg/L. The stock solution was delivered to the test chambers via a diluter system where it prepared test treatments at nominal hexanol levels of 0, 41, 68, 113, 189, and 315 mg/L. Measured concentrations were 0, 26.7, 49.2, 90.6, 170.0, and 261.5 mg/L. Fifty fish, divided into two replicates, were tested at each concentration level. The 96-hour LC_{50} was 97.7 mg/L based on measured values (Brooke, et al, 1984). The acute toxicity of the analogue substance 1-hexanol was also investigated with *Pimephales promelas* following the USEPA test procedures described above. The 96-hour LC_{50} was 97.5 mg/L based on measured values (Veith, et al, 1983).

Experimental data for the acute toxicity of hexanol, branched and linear to aquatic invertebrates are not available. Using the ECOSAR computer model (Cash and Nabholz, 1990) a 48-hour EC_{50} of 137 mg/L was calculated. Results of modeling for C7, C8, and C9 branched alcohols are consistent with the experimental data used to characterize the acute toxicity of the C6-8 and C7-9 branched alcohols, as well as the C8-10 iso, C9 rich alcohol product (Table 6). This suggests that the ECOSAR model is sufficiently robust to accurately calculate the toxicity for this range of chemicals. Therefore, the modeled value for a C6 alcohol is expected to be consistent with an experimental value for hexanol, branched and linear.

An acute experimental value is also reported for a freshwater green alga (*Pseudokirchneriella subcapitata*). Hexanol, branched and linear was tested following OECD 201 test guidelines. Individual WAFs were prepared at nominal levels of 0, 6, 14, 34, 82, and 196 mg/L in algal nutrient media. Each test replicate was inoculated with 1.0×10^4 algal cells/mL and placed on an oscillating table under continuous lighting. Under static conditions, the 72-hour EC_{50} values based on biomass and growth rate were 89 and 159 mg/L, respectively, with corresponding No Observed Effect Concentrations (NOEC) values of 5 and 35 mg/L, respectively (EMBSI, 2003b).

Alcohols C6-C8, branched (CAS 70914-20-4)

The acute toxicity of Alcohols C6-C8 branched was investigated with a freshwater fish (*Pimephales promelas*) following test procedures developed by the USEPA. The study was conducted under flow-through conditions. A stock solution was prepared at a nominal concentration of 1400 mg/L. The stock solution was delivered to the test chambers via a diluter system where it prepared test treatments at nominal heptanol levels of 0, 12.5, 19.3, 29.7, 45.7, and 70.3 mg/L. Measured concentrations were 0, 12.5, 18.1, 28.5, 43.6, and 70.8 mg/L. Twenty fish were tested at each concentration level. The 96-hour LC_{50} was 34.5 mg/L based on measured values (Geiger, et al, 1986).

Alcohols C6-C8 branched was also investigated for its effects on the freshwater invertebrate (*Daphnia magna*) following concept rules of the Dutch Standardization Institute (Adema, 1978). Tests using n-heptanol were conducted concurrently at two different laboratories in the Netherlands using test organisms supplied by in-house cultures. The 48-hour EC_{50} was 63 mg/L, and was based on nominal concentrations of the test substance (Canton and Adema, 1978).

Alcohols C7-C9-iso, C8 rich (CAS# 68526-83-0)

The acute toxicity of Alcohols C7-9 iso, C8 rich was investigated with a freshwater fish (*Pimephales promelas*) following test procedures developed by the USEPA. The study was conducted under flow-through conditions. A stock solution was prepared at a nominal concentration of 275 mg/L. The stock solution was delivered to the test chambers via a diluter system where it prepared test treatments at

nominal octanol levels of 0, 8.6, 10.8, 13.5, 16.9, and 21.1 mg/L. Measured concentrations were 0, 8.8, 10.7, 12.7, 16.5, and 20.4 mg/L. Twenty fish were tested at each concentration level. The 96-hour LC_{50} was 14.0 mg/L based on measured values (Geiger, et al, 1988). The acute toxicity of the analogue substance 1-octanol was also investigated with *Pimephales promelas* following the USEPA test procedures described above. The 96-hour LC_{50} was 13.5 mg/L based on measured values (Brooke, et al, 1984).

Alcohols C7-9 iso, C8 rich was also investigated for its effects on the freshwater invertebrate (*Daphnia magna*) following USEPA 660/3-75-009 Environmental Effects test guidelines. The study was conducted under static conditions. Individual treatments were prepared by adding varying amounts of the test substance directly to 250 ml of dilution water in glass beakers. Four replicates were prepared at each treatment level. Nominal levels were 0, 10, 18, 32, 56, 100 and 180 mg/L. The 48-hour EC_{50} was 31.8 mg/L based on nominal loading levels (Union Carbide, 1980).

Nonanol (CAS# 28473-21-4)

No experimental data are available.

Estimated values for acute toxicity to invertebrates and green algae were calculated using the ECOSAR computer model (Cash and Nabholz, 1990). The estimated 48-hour EC_{50} value for acute toxicity to daphnia was 7.5 mg/L. The estimated 96-hour EC_{50} vaue for acute toxicity to green algae was 5.1 mg/L. As discussed previously, the ECOSAR computer model is sufficiently robust to accurately calculate the potential toxicity for this chemical category.

Alcohols C8-C10-iso, C9 rich (CAS 68526-84-1)

The acute toxicity of Alcohols C8-C10-iso, C9 rich was investigated with a freshwater fish (*Oncorhynchus mykiss*) following OECD 203 test guidelines. The study was conducted using static-renewal procedures with approximately 80% of the test solution in each test replicate renewed at 24-hour intervals. The 96-hour LC_{50} was 10.1 mg/L (EMBSI, 1996b).

Alcohols C8-C10-iso, C9 rich was also investigated for its effects on the freshwater invertebrate (*Daphnia magna*) following OECD 202 test guidelines. Under static conditions, the study reported a 48-hour EC_{50} of 4.9 mg/L (EMBSI, 1996c).

Alcohols C9-C11-iso, C10 rich (CAS 68526-85-2)

The acute toxicity of Alcohols, C9-C11-iso, C10 rich was investigated with a freshwater fish (*Oncorhynchus mykiss*) following OECD 203 test guidelines. The study was conducted using static-renewal procedures with approximately 80% of the test solution in each test replicate renewed at 24-hour intervals. The 96-hour LC_{50} was 3.1 mg/L (EMBSI, 1996d). The acute toxicity of the analogue substance 1-decanol was investigated with the fathead minnow (*Pimephales promelas*) following USEPA flow-through test procedures. The test substance was delivered to the test chambers via a diluter system. The 96-hour LC_{50} was 2.4 mg/L based on measured values (Veith, et al, 1983).

Alcohols, C9-C11-iso, C10 rich was also investigated for its effects on the freshwater invertebrate (*Daphnia magna*) following methods comparable to OECD 202 test guidelines. Under static conditions, the study reported a 48-hour EL_{50} of 6.2 mg/L (EG&G, 1982).

Alcohols C11-C14 iso, C13 rich (CAS 68526-86-3)

The acute toxicity of Alcohols C11-C14-iso, C13 rich was investigated with a freshwater fish (*Oncorhynchus mykiss*) following OECD 203 test guidelines. The study was conducted using static-renewal procedures with approximately 80% of the test solution in each test replicate renewed at 24-hour intervals. The 96-hour LC_{50} was 0.42 mg/L (EMBSI, 1998e).

Acute experimental values are also reported for Alcohols C11-C14-iso, C13 rich using *Daphnia magna*. The studies were performed under static conditions following OECD 202 test guidelines and resulted in 48-hour EC_{50} values of 0.81 and 0.71 mg/L (EMBSI, 1987, 1997c).

An acute experimental value was also reported for the freshwater alga (*Pseudokirchneriella subcapitata*). Alcohols C11-C14-iso, C13 rich was tested following OECD 201 test guidelines using *P. subcapitata*. The 72-hour EC_{50} values based on biomass and growth rate were 2.6 and 3.2 mg/L, respectively, with corresponding NOEC values of 1.5 and 2.2 mg/L (EMBSI, 2003c).

Table 7. Acute aquatic toxicity of members of the Alkyl Alcohols C6-C13 Category (ECOSAR modeled data indicated by shaded area).

Substance (CAS #)	Hexanol, branched and linear (68526-79-4)	Alcohols C6-8, Branched (70914-20-4)	Alcohols C7-9 iso, C8 rich (68526-83-0)	Nonanol (28473-21-4)	Alcohols C8-10 iso, C9 rich (68526-84-1)	Alcohols C9-11 iso, C10 rich (68526-85-2)	Alcohols C11-14 iso, C13 rich (68526-86-3)
FISH ACUTE TOXICITY (96-hour)	LC_{50}= 97.7 mg/L (Brooke, 1984)	LC_{50}= 34.5 mg/L (Geiger, 1986)	LC_{50}= 14.0 mg/L (Geiger, 1988)	RA	LC_{50}= 10.1 mg/L (EMBSI, 1996b)	LC_{50}= 3.1 mg/L (EMBSI, 1996d)	LC_{50}= 0.42 mg/L (EMBSI, 1998e)
FISH ACUTE TOXICITY (96-hour)	C6 OH LC_{50}= 130 mg/L	C7 OH LC_{50}= 51 mg/L	C8 OH LC_{50}= 20 mg/L	C9 OH LC_{50}= 6.4 mg/L	C9 OH LC_{50}= 7.6 mg/L	C10 OH LC_{50}= 3.1 mg/L	C13 OH LC_{50}= 0.2 mg/L
***DAPHNID* ACUTE TOXICITY (48-hour)**	RA	LC_{50}= 63 mg/L (Canton, 1978)	LL_{50}= 31.8 mg/L (Union Carbide, 1980)	RA	LC_{50}= 4.9 mg/L (EMBSI, 1996c)	LC_{50}= 6.2 mg/L (EG&G, 1982)	LC_{50}= 0.71 mg/L (EMBSI, 1987)
***DAPHNID* ACUTE TOXICITY (48-hour)**	C6 OH LC_{50}= 137 mg/L	C7 OH LC_{50}= 56 mg/L	C8 OH LC_{50}= 22 mg/L	C9 OH LC_{50}= 7.5 mg/L	C9 OH LC_{50}= 8.9 mg/L	C10 OH LC_{50}= 3.5 mg/L	C13 OH LC_{50}= 0.2 mg/L
ALGA TOXICITY (96-hour)	EC_{50}= 89 mg/L (EMBSI, 2003b)*	RA	RA	RA	RA	RA	EC_{50}= 2.6 mg/L (EMBSI, 2003c)*
ALGA TOXICITY (96-hour)	C6 OH EC_{50}= 84 mg/L	C7 OH EC_{50}= 35 mg/L	C8 OH EC_{50}= 15 mg/L	C9 OH EC_{50}= 5.1 mg/L	C9 OH EC_{50}= 6.0 mg/L	C10 OH EC_{50}= 2.4 mg/L	C13 OH EC_{50}= 0.15 mg/L

RA read across
OH alcohol
* 72-hour test

Figure 2: Acute Aquatic Toxicity of Alkyl Alcohols C6 to C13 by Carbon Number

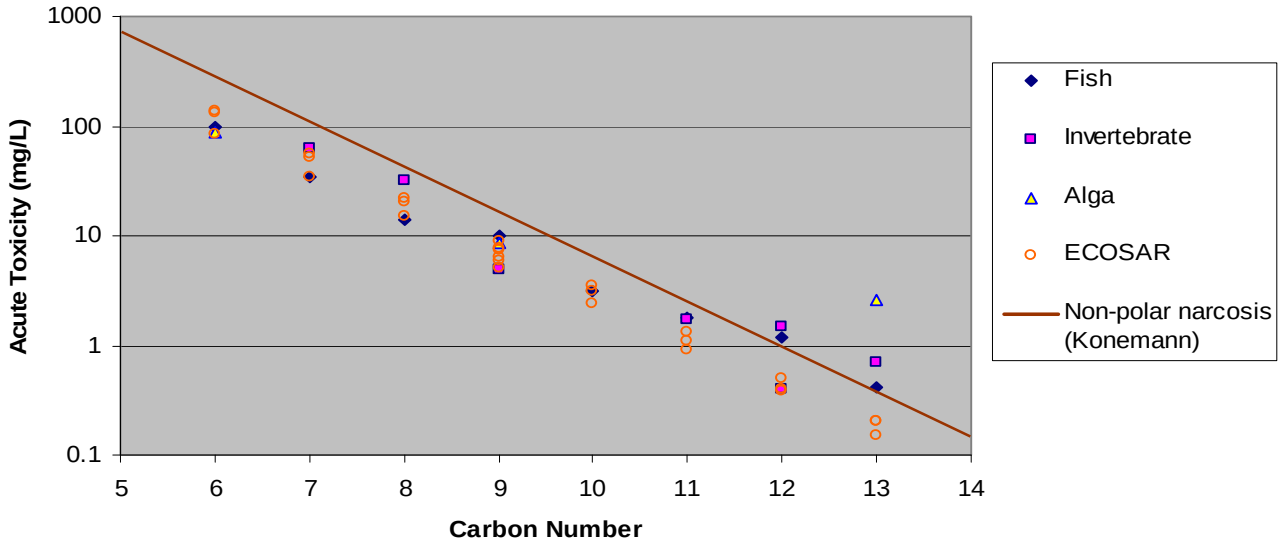


Figure 2 illustrates the trend in acute aquatic toxicity exhibited by members of the Alkyl Alcohols C6 to C13 Category and includes additional data for a C11 and C12 alcohol that are presented to further support this trend and justify consideration of the seven alcohols as a category. The C11 and C12 alcohols are not members of the category, but the data are useful in confirming the toxicity trend for this category. Figure 2 also includes acute aquatic toxicity values estimated using the ECOSAR computer model (Cash and Nabholz, 1990). The values represent acute aquatic toxicity for freshwater fish, invertebrates, and green algae and are included to illustrate the robustness of the model and its ability to estimate toxicity for this category of chemicals. Specific results can also be found in Table 7.

Despite the variability in the data, the figure clearly shows that as carbon number increases from a C6 to a C13, toxicity increases as is expected for non-polar narcotics. The trend line illustrates the results for the Koenemann QSAR for non-polar narcosis (Koenemann, 1981).

Chronic Toxicity Test Results

Experimental chronic toxicity data for category members are not available. Chronic aquatic toxicity values were calculated using the ECOSAR computer model (Cash and Nabholz, 1990). Calculated chronic values for category members include 30-day fish values that range from 16.1 to 0.03 mg/L, 16-day invertebrate values that range from 6.3 to 0.04 mg/L, and 96-hour alga values that range from 7.3 to 0.1 mg/L (Table 7). However, the substances in this category have a low potential for chronic exposure of aquatic organisms based on a moderate to rapid rate of biodegradability. As a result, long-term adverse effects to aquatic organisms are not expected given a non-continuous (e.g. accidental release) emission source.

Table 7. Chronic aquatic toxicity of members of the Alkyl Alcohols C6-C13 Category (calculated by the ECOSAR computer model).

Substance (CAS #)	Hexanol, branched and linear (68526-79-4)	Alcohols C6-8, Branched (70914-20-4)	Alcohols C7-9 iso, C8 rich (68526-83-0)	Nonanol (28473-21-4)	Alcohols C8-10 iso, C9 rich (68526-84-1)	Alcohols C9-11 iso, C10 rich (68526-85-2)	Alcohols C11-14 iso, C13 rich (68526-86-3)
FISH ACUTE TOXICITY (30-day)	ChV = 16.1 mg/L	ChV = 6.8 mg/L	ChV = 2.9 mg/L	ChV = 1.0 mg/L	ChV = 1.2 mg/L	ChV = 0.5 mg/L	ChV = 0.03 mg/L
***DAPHNID* ACUTE TOXICITY (16-day)**	EC_{50}= 6.3 mg/L	EC_{50}= 3.2 mg/L	EC_{50}= 1.6 mg/L	EC_{50}= 0.7 mg/L	EC_{50}= 0.8 mg/L	EC_{50}= 0.4 mg/L	EC_{50}= 0.04 mg/L
ALGA TOXICITY (96-hour)	ChV = 7.3 mg/L	ChV = 4.1 mg/L	ChV = 2.2 mg/L	ChV = 1.1 mg/L	ChV = 1.2 mg/L	ChV = 0.6 mg/L	ChV = 0.09 mg/L

ChV = Chronic Value

4.2 Terrestrial Effects

Acute Toxicity Test Results

There are no experimental data available using standard testing procedures that can be used to assess the terrestrial hazard of members of the Alkyl Alcohols C6 to C13 Category. However, there are calculated (ECOSAR) earthworm 16-day LC50 values that range from 128 to 880 mg/kg soil (Cash and Nabholz, 1990). These values were calculated using log K_{ow}, water solubility, and melting point values from Table 1. The modelled earthworm data would suggest that category members would have a low order of toxicity to soil dwelling organisms.

4.3 Other Environmental Effects

Data on other environmental effects are not available.

4.4 Assessment Summary for the Environment

Results of the Mackay Level III environmental distribution model suggest a high environmental distribution into the water compartment for alcohols with a carbon chain length of C6 to C10. The model also predicts a high environmental distribution into the sediment compartment for alcohols C11-C14-iso, C13 rich. Volatilization to the air from aqueous and terrestrial habitats will be negligible because Alkyl Alcohols C6 to C13 have low vapor pressure (<2.59 hPa at 25° C). Indirect photo-degradation of Alkyl Alcohols C6 to C13 Category substances can occur at a rapid rate, however, based on their low vapor pressure it is not expected to contribute significantly to their degradation in the environment. Aqueous photolysis and hydrolysis are also not expected to contribute to the transformation of the alkyl alcohols in aquatic environments because they are either poorly or not susceptible to these reactions.

Biodegradability of the Alkyl Alcohols C6 to C13 Category members has been evaluated with standard 28-day test guidelines. The results from these studies suggest that the members of the Alkyl Alcohols C6 to C13 Category are subject to microbial degradation under aerobic conditions and are either readily biodegradable or rapidly biodegrade.

The predominant mechanism accounting for removal in a wastewater treatment facility is biodegradation, followed by partitioning to sludge, with volatilization accounting for the remaining loss.

Member substances of the Alkyl Alcohols C6 to C13 Category have been shown to exhibit moderate to high acute aquatic toxicity. This assessment is supported by the results of aquatic toxicity studies for various organisms covering the three trophic levels. Experimental acute toxicity values for fish and invertebrates range from 0.42 to 97.7 mg/L, and 0.71 to >63 mg/L, respectively. For algae, the experimental 72-hr EC_{50} ranges from 2.6 to 89.0 mg/L. Despite some variability, the acute aquatic toxicity data clearly shows that as carbon number increases from C6 to C13, the toxicity increases as is expected for non-polar narcotics. Experimental results with linear analogue further support this trend. Experimental chronic toxicity data for category members are not available. Calculated chronic toxicity values range from 16.1 to 0.03 mg/L for the three trophic levels.

Category members have a low potential to bioaccumulate in aquatic species based biochemical evidence of biotransformation and on experimentally derived bioconcentration factors (BCF) in fish in the range of 15 to 60 L/kg wet.

In the terrestrial environment, category members are expected to exhibit a low order of toxicity based on calculated 14-day earthworm LC_{50} values ranging from 128 to 880 mg/kg soil.

5 RECOMMENDATIONS

Human Health

The chemicals in the Alkyl Alcohols C6 to C13 Category are currently of low priority for further work. They possess properties indicating a low hazard for human health, except for eye and skin irritation. These reversible effects should be noted by health professionals and users. No further testing is required.

Environment

The chemicals in this category with chain lengths of C6 through C10 are of low priority for further work. They have properties indicating a hazard for the environment (acute aquatic EC/LC_{50} values between 1 and 100 mg/l). However they are of low priority for further work for the environment because of their rapid biodegradation and their limited potential for bioaccumulation

However, as C13 members show acute aquatic effects at concentrations below 1 mg/l, they should be candidates for further work.

However, the members in the category are currently of low priority for further work due to ready or inherent biodegradation and low potential for bioaccumulation.

6 DATA SUMMARY

Physico-chemical, environmental fate and effects, and human health data that characterize the seven products in the Alkyl Alcohols C6 to C13 Category are summarized in Tables 8 and 9.

Table 8. PhysChem and Environmental Data Summary

Endpoint	Alkyl Alcohols C6 to C13 Category CAS RNs						
	Hexanol, branched and linear	**Alcohols C6-8, Branched**	**Alcohols C7-9 iso, C8 rich**	**Nonanol**	**Alcohols C8-10 iso, C9 rich**	**Alcohols C9-11 iso, C10 rich**	**Alcohols C11-14 iso, C13 rich**
	68526-79-4	**70914-20-4**	**68526-83-0**	**28473-21-4**	**68526-84-1**	**68526-85-2**	**68526-86-3**
Melting Point (°C)	-49.3	-37.2	-65	-18.7	-54	-40	<-40
Boiling Range (°C)	152 to 163	167 to 176	185 to 193	192 to 204	202 to 219	216 to 226	250 to 270
Vapor Pressure (hPa)	2.56	0.58	2.59	0.40	0.054	0.018	0.002
Log K_{ow} Range	1.8 to 2.0	1.8 to 2.6	2.9 to 3.4 (m)	3.2 to 4.9 (m)	3.8 to 4.3 (m)	4.2 to 4.3 (m)	4.8 to 5.5 (m)
Water Solubility Range (mg/L)	10,340 to 11,950	3,539 to 11,950	1,379 to 1,485	128 (m)	90.4	75.0 (m)	5.8 (m)
Direct Photodegradation	Direct photolysis will not contribute to degradation						
Indirect (OH-) Photodegradation (half-life, hrs) (a)	12.8	11.5	10.2	9.2	9.2	6.0	6.5
Hydrolysis	Hydrolysis will not contribute to degradation						
Distribution	Predominantly in water						Predominantly in sediment

(m) Measured values
(a) Atmospheric half-life values are based on a 12-hr day

Table 8. Continued

Endpoint	Alkyl Alcohols C6 to C13 Category CAS RNs						
	Hexanol, branched and linear	**Alcohols C6-8, Branched**	**Alcohols C7-9 iso, C8 rich**	**Nonanol**	**Alcohols C8-10 iso, C9 rich**	**Alcohols C9-11 iso, C10 rich**	**Alcohols C11-14 iso, C13 rich**
	68526-79-4	**70914-20-4**	**68526-83-0**	**28473-21-4**	**68526-84-1**	**68526-85-2**	**68526-86-3**
Biodegradation (% after 28 days)	>82 (ra)		82	84	71 to 84 (ra)	71	60.6
96-hr Fish LC_{50} (mg/L)	97.7	34.5	14.0	10.1 to 14.0 (ra)	10.1	3.1	0.42
48-hr Invertebrate EC_{50} (mg/L)	> 63 (ra)	63	31.8	4.9 to 31.8 (ra)	4.9	6.2	0.71
96-hr Alga EC_{50} (mg/L)	89 b 159 gr	2.6 to 89 b (ra) 3.2 to 159 gr (ra)					2.6 b 3.2 gr
96-hr Alga NOEC (mg/L)	5 b 35 gr	1.5 to 5 b (ra) 2.2 to 35 gr (ra)					1.5 b 2.2 gr

b = biomass
r = growth rate
ra = based on read-across data from other members of the category or analogue substances.

Table 9. Human Health Data Summary

Endpoint	Alkyl Alcohols C6 to C13 Category CAS RNs						
	Hexanol, branched and linear	**Alcohols C6-8, Branched**	**Alcohols C7-9 iso, C8 rich**	**Nonanol**	**Alcohols C8-10 iso, C9 rich**	**Alcohols C9-11 iso, C10 rich**	**Alcohols C11-14 iso, C13 rich**
	68526-79-4	**70914-20-4**	**68526-83-0**	**28473-21-4**	**68526-84-1**	**68526-85-2**	**68526-86-3**
Acute Oral Toxicity (rat)	3.7 g/kg	>3.9 g/kg	>2 g/kg		3 g/kg	4.6 g/kg	>2 g/kg
Acute Dermal Toxicity (rabbit)	>2.6 g/kg	>3.16 g/kg	>2.6 g/kg		>3.16 g/kg	>2.6 g/kg	
Irritation	Severe irritant (eyes) Moderate irritant (skin)	Severe irritant (eyes) Moderate irritant (skin)	Severe irritant (eyes) Moderate irritant (skin)	Severe irritant (eyes) (ra) Moderate irritant (skin) (ra)	Severe irritant (eyes) Moderate irritant (skin)	Severe irritant (eyes) Moderate irritant (skin)	Moderate irritant (eyes) Moderate irritant (skin)
Mutagenicity Ames Assay	Negative	Negative (ra)	Negative	Negative (ra)			Negative
Mutagenicity Mouse Micronucleus	Negative (ra)		Negative	Negative (ra)			Negative
Repeat Dose Toxicity (rat)	NOAEL = 130 mg/kg/day (ra)		NOAEL = 125 mg/kg/day (ra)	NOAEL = 144 mg/kg/day (ra)		NOAEL = 168 mg/kg/day (ra)	NOAEL = 184 mg/kg/day (ra)
Carcinogenicity	Negative (ra)						
Reproductive Toxicity (rat)	NOAEL = 144 mg/kg/day (ra)			NOAEL = 144 mg/kg/day		NOAEL = 168 mg/kg/day (ra)	
Developmental Toxicity (rat) NOAEL (mg/kg/day)	(fm = 3500 (ra) (f) = 3500 (ra) NOAEL in mg/m^3	(m) ≥ 500 (ra) (f) ≥1000 (ra)	(m) = 500 (f) = 1000	(m) = 144 (ra) (f) = 144 (ra)		(m) = 158 (ra) (f) = 790 (ra)	(m) = 250 (ra) (F) = 750 (ra)

(ra) Based on read-across data from other members of the category or analog substances.

(m) maternal (f) fetal

7 REFERENCES

- Adema, D.M.M. (1978). Daphnia magna as Test Organisms in Acute and Chronic Toxicity Experiments. Hydrobiologica 59(2): 125-134.
- Banduhn N. (1992). Henkel KGaA. Unpublished data. Archive No. RT-92162.
- Barylak IR and Kosaschuk SJ (1988). Tsitol. Genet. 22, 49-52.
- BASF (1991). Report on the Oral Toxicity of 2-ethylhexanol in Rats After the Administration by Gavage (Aqueous Emulsion) for Three Months. Project No. 31C0631 / 87077. Cited in EPA OTS 0529872.
- BioDynamics (1980). Eye Irritation Study in Rabbits. Unpublished report.
- Boethling, R.S., Mackay, D. (2000). Handbook of Property Estimation Methods for Chemicals. CRC Press, Boca Raton, FL, USA.
- Brooke, L.T., D.J. Call, Geiger, D.L. and C.E. Northcott, (1984). "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol. 1. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior, Superior, WI. Pp. 179-180.
- Canton, J.H., and D.M.M. Adema. (1978). "Reproducibility of Short-term and Reproduction Toxicity Experiments with *Daphnia magna* and Comparison of the Sensitivity of *Daphnia magna* with *Daphnia pulex* and *Daphnia cucullata* in Short-term Experiments." Hydrobiologica 59(2): 135-140.
- Cash G and Nabholz V (1990). ECOSAR. U.S. Environmental Protection Agency, Office of Pesticide, Pollution, and Toxics - Risk Assessment Division. Washington, DC, USA.
- Clayton G and Clayton F (eds.) (1994). Patty's industrial hygiene and toxicology, Vol. 2D, 4th Edition, John Wiley & Sons, New York, USA.
- De Wolf, W. and T.F. Parkerton (1999). Higher alcohols bioconcentration: Influence of biotransformation. Extended Abstracts of the 217th ACS National Meeting, Anaheim, CA, Symposium "Persistent, Bioaccumulative, Toxic Chemicals, March 21-25, 1999.
- ECB (2000a). European Chemicals Bureau - IUCLID dataset for hexan-1-ol (CAS RN 111-27-3). 10.02.2000.
- ECB (2000b). European Chemicals Bureau - IUCLID dataset for 2-ethylhexan-1-ol (CAS RN 104-76-7). 10.02.2000.
- EG&G Bionomics (1982). Acute toxicity of MRD-82-04 to the water flea (*Daphnia magna*). Report No. BW-82-7-1217.
- Egorov, YuL and Adrianov LA, Uch. Zap. Mosk. Nauchn. - Issled Inst. Gig. 9, 47, (1961), In: Chemical Abstracts, 61, 3601 (1964) und 60, 12576d (1964), In: Clayton GD and Clayton FE (eds), Patty's Industrial Hygiene and Toxicology, Third Revised Edition in Three Volumes, Volumes 2A, 2B and 2C, Toxicology, New York (1982).
- EPIWIN (1999). Estimation Program Interface for Windows, version 3.12. Syracuse Research Corporation, Syracuse, NY, USA.
- Esso Research and Engineering (1960a). Unpublished report.

- Esso Research and Engineering (1960b). Acute dermal toxicity of isodecanol in rabbits. Unpublished report.
- Esso Research and Engineering (1961). Repeat dermal application of Alcohols, C7-9 branched. Unpublished report.
- Esso Research and Engineering (1968a). Acute oral administration-rats. Project No. 145-340. Unpublished report.
- Esso Research and Engineering (1968b). Acute inhalation exposure mice, rats, guinea pigs. Project No. 145-340. Unpublished report.
- Esso Research and Engineering (1968c). Acute dermal and eye application - rabbits. Project No. 145-340. Unpublished report.
- Esso Research and Engineering (1970). Acute eye application - rabbits. Project No. 145-458. Unpublished report.
- Esso Research and Engineering (1979). Acute Oral Toxicity Study in Rats. Unpublished report.
- Exxon Research and Engineering (1979a). Test for Acute Dermal Toxicity/LD_{50} in Rabbits. Unpublished report.
- Exxon Research and Engineering (1979b). Test for Eye Irritation in Rabbits. Unpublished report.
- EMBSI. (1987). ExxonMobil Biomedical Sciences, Inc. Static acute Daphnia toxicity test. Study No. 269342. Unpublished report.
- EMBSI. (1992). ExxonMobil Biomedical Sciences, Inc. Primary dermal irritation study in the rabbit. Study No. 112704. Unpublished report.
- EMBSI. (1993). ExxonMobil Biomedical Sciences, Inc. Upper airway sensory irritation study in mice. Study No. 140751. Unpublished report.
- EMBSI. (1994a). ExxonMobil Biomedical Sciences, Inc. Microbial Mutagenesis in Salmonella Mammalian Microsome Plate Incorporation Assay with C7-C9 Branched Alkyl Acetate Ester. Unpublished report.
- EMBSI. (1994b). ExxonMobil Biomedical Sciences, Inc. Microbial Mutagenesis in Salmonella Mammalian Microsome Plate Incorporation Assay with C11-C14 Branched Alkyl Acetate Ester. Unpublished report.
- EMBSI. (1994c). ExxonMobil Biomedical Sciences, Inc. Developmental Toxicity Study in Rats. Unpublished report.
- EMBSI. (1995a). ExxonMobil Biomedical Sciences, Inc. Microbial Mutagenesis in Salmonella Mammalian Microsome Plate Incorporation Assay with C6 Branched and Linear Alkyl Acetate Ester. Unpublished report.
- EMBSI. (1996a). ExxonMobil Biomedical Sciences, Inc. Ready biodegradability: OECD 301F manometric respirometry test. Study No. 114794A. Unpublished report.
- EMBSI. (1996b). ExxonMobil Biomedical Sciences, Inc. Fish acute toxicity test. Study No. 114858. Unpublished report.
- EMBSI. (1996c). ExxonMobil Biomedical Sciences, Inc. Acute toxicity for Daphnia. Study No. 149542. Unpublished report.

- EMBSI. (1996d). ExxonMobil Biomedical Sciences, Inc. Fish acute toxicity test. Study No. 114958. Unpublished report.
- EMBSI. (1997a). ExxonMobil Biomedical Sciences, Inc. Ready biodegradability: OECD 301F manometric respirometry test. Study No. 114994A. Unpublished report.
- EMBSI. (1997b). ExxonMobil Biomedical Sciences, Inc. Ready biodegradability: OECD 301F manometric respirometry test. Study No. 195994A. Unpublished report.
- EMBSI. (1997c). ExxonMobil Biomedical Sciences, Inc. Acute toxicity for Daphnia. Study No. 118542. Unpublished report.
- EMBSI. (1998). ExxonMobil Biomedical Sciences, Inc. N-Octanol/water partition coefficient. Study No. 193387D. Unpublished report.
- EMBSI. (1998a). ExxonMobil Biomedical Sciences, Inc. Ready biodegradability: OECD 301F manometric respirometry test. Study No. 174194A. Unpublished report.
- EMBSI. (1998b). ExxonMobil Biomedical Sciences, Inc. Ready biodegradability: OECD 301F manometric respirometry test. Study No. 180294A. Unpublished report.
- EMBSI. (1998c). ExxonMobil Biomedical Sciences, Inc. Bioconcentration: flowthrough fish test. Study No. 114947. Unpublished report.
- EMBSI. (1998d). ExxonMobil Biomedical Sciences, Inc. Product Stewardship Risk Assessment: Exxal Alcohols.
- EMBSI. (1998e). ExxonMobil Biomedical Sciences, Inc. Fish acute toxicity test. Study No. 118558. Unpublished report.
- EMBSI. (1999a). ExxonMobil Biomedical Sciences, Inc. Bioconcentration: flowthrough fish test. Study No. 118347. Unpublished report.
- EMBSI. (2003a). ExxonMobil Biomedical Sciences, Inc. Ready Biodegradability of Alcohols and Alcohol Ethoxylates. Unpublished report.
- EMBSI. (2003b). ExxonMobil Biomedical Sciences, Inc. Alga, Growth Inhibition Test. Study No. 140867. Unpublished report.
- EMBSI. (2003c). ExxonMobil Biomedical Sciences, Inc. Alga, Growth Inhibition Test. Study No. 140967. Unpublished report.
- EMBSI. (2005a). ExxonMobil Biomedical Sciences, Inc. personal communication.
- EMBSI. (2005b). ExxonMobil Biomedical Sciences, Inc. In Vitro Chromosomal Aberration Assay in CHO Cells. Study No. 0407927. Unpublished report.
- ExxonMobil Chemical Company (2001a). Intermediates Product Assessment - Exxal 8 Unpublished Data.
- ExxonMobil Chemical Belgium (2003a). Intermediates Product Assessment - Isononanol Unpublished Data.
- ExxonMobil Chemical Belgium (2003b). Intermediates Product Assessment - Isodecanol Unpublished Data.
- ExxonMobil Chemical Belgium (2003c). Intermediates Product Assessment - Isotridecanol

Unpublished Data.

- ExxonMobil Chemical Company (2003d). Intermediates Product Assessment - Isohexanol Unpublished Data.
- ExxonMobil Chemical Company (2003e). Intermediates Product Assessment - Isoheptanol Unpublished Data.
- Falbe J, Bahrmann H, Lipps W, Isny G, and Mayer D, in *Ullman's Encyclopedia of Industrial Chemistry*, 5th completely revised ed., Vol. A1, VCH Publishers, 1984, pp. 279-303.
- Fraunhofer Institute (1993). FH-ITA Study No. 91/10 CM.
- Geiger, D.L., S.H. Poirier, L.T. Brooke, and D.J. Call. (1986). "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol. 3. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior, Superior, WI. Pp. 181-182.
- Geiger, D.L., D.J. Call, and L.T. Brooke. (1988). "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol. 4. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior, Superior, WI. Pp. 183-184.
- Hansen E. (1992). Combined repeat dose and reproductive/developmental toxicity screening test on 1-dodecanol in rats. Institute of Toxicology, Danish National Food Agency. IT 9211105.
- Harris J (1982). Rate of Hydrolysis. In: Handbook of Chemical Property Estimation Methods. Environmental Behavior of Organic Compounds. 7, 1-48. Lyman W, Reehl W and Rosenblatt D (eds.). McGraw Hill, New York, NY, USA.
- Hazleton Labs (1960) "Acute oral, acute dermal, and acute inhalation toxicity of Hexyl alcohol, Isoheptyl alcohol, and Isooctyl Alcohol." Unpublished report.
- Hellwig J and Jaeckh R (1997). Differential prenatal toxicity of one straight-chain and five branched-chain primary alcohols in rats, Food Chem. Toxicol., 35: 489-500.
- Koenemann, H. (1981). Quantitative structure-activity relationships in fish toxicity studies. 1. Relationship for 50 industrial pollutants. Toxicol. 19: 201-220.
- Letinski D, Connelly Jr. M, Peterson D and Parkerton T (2002). Slow-stir water solubility measurements of selected alcohols and diesters. Chemosphere 48, 257-265.
- Lington AW and Bevan C. (1994). Patty's Industrial Hygiene and Toxicology, Fourth Edition, John Wiley & Sons, Inc, Chapter Thirty, "Alcohols," pp. 2585-2710.
- Lipnick, R.L., D.E. Johnson, J.H. Gilford, C.K. Bickings, L.D. Newsome (1985). Comparison of fish toxicity screning data for 55 alcohols with the quantitative structure-activity relationship predictions of minimum toxicity for nonreactive nonelectrolyte organic compounds. Environ. Tox. and Chem (4): 281-296.
- Mann A.H. (1987). An assessment of the likely metabolic fate of some isomers of hexyl acetate. The Robins Institute of Industrial & Environmental Safety, University of Surrey, Guildford Surrey, U.K.
- Mackay D, Di Guardo A, Paterson S and Cowan C (1996). Evaluating the environmental fate of a variety of types of chemicals using the EQC model. Environ. Toxicol. Chem. **15**:1627-1637.
- Mackay D, DiGuardo A, Paterson S and Cowan C (2003). EQC Model version 2.02, available from

the Environmental Centre, Trent University, Canada.

- Meylan W and Howard P (1993). Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere **26**:2293-2299.
- Monick, JA (1968). Alcohols. Their Chemistry, Properties and Manufacture. Reinhold Book Corporation, NY.
- Nelson B, Brightwell W, Khan A, Krieg E Jr and Hoberman A (1989). Developmental toxicology evaluation of 1-Pentanol, 1-Hexanol, and 2-ethyl-1-hexanol administered by inhalation to rats. Journal of the American College of Toxicology **8** (2): 405-410. NIOSH, Division of Biomedical and Behavioral Sciences.
- Nelson B, Brightwell W, Khan A, Krieg E Jr and Hoberman A (1990). Developmental toxicology assessment of 1-Octanol, 1-Nonanol, and 1-Decanol administered by inhalation to rats. Journal of the American College of Toxicology **9** (1): 93-97. NIOSH, Division of Biomedical and Behavioral Sciences.
- OECD (2004). Guidance Document on the Use of Multimedia Models for Estimating Overall Environmental Persistance and Long-Range Transport, OECD Series on Testing and Assessment No. 45.
- RCC Research and Consulting Co. AG (1988a). Acute oral toxicity study with Alcohols, C7-9 branched in rats. Unpublished report.
- RCC. Research and Consulting Company (1988b). Acute oral toxicity study with alcohols, C11-C14 iso, C13 rich in rats. Unpublished report.
- RCC. Research and Consulting Company (1988b). Eye irritation (rinsed/unrinsed) in the rabbit after single application with Exxal 13. RCC Project No. 207145. Unpublished report.
- RCC. Research and Consulting Company (1989). Primary skin irritation study with Exxal 13 in rabbits. RCC Project No. 207134. Unpublished report.
- Rhodes C, Soames T, Stonard M, Simpson M, Vernall A and Elcombe C (1984). The absence of testicular atrophy and in vivo and in vitro effects on hepatocyte morphology and peroxisomal enzyme activities in male rats following the administration of several alkanols. Toxicology Letters 21, 103-109.
- Safepharm Laboratories, Ltd. (1993a). Exxal 13 (C13 alcohol) acute dermal irritation test in the rabbit. Project No. 616/2. Unpublished data.
- Safepharm Laboratories, Ltd. (1993b). Exxal 9 (C9 alcohol) acute eye irritation test in the rabbit. Project No. 616/1. Unpublished data.
- Scala R and Burtis E 1973. Acute toxicity of a homologous series of branched chain primary alcohols. Am. Ind. Hyg. Assoc. J. **34**: 493-499.
- Shimizu H, Suzuki Y, Takemura N, Goto S and Matsushita H (1985). The results of microbial mutation test for forty-three industrial chemicals. Japanese Journal of Industrial Health 27: 400-419.
- Treon JF unpublished data, In: Patty F.A. (ed.). Industrial Hygiene and Toxicology, Second revised edition, Volume II, Toxicology, Fassett DW and Irish DD (eds), Interscience Publishers, New York, London, Sydney (1962).

- TSCATS (1991a), OTS 0524017-2, Doc I.D. 89-910000247, 8E, sanitized, 19.04.1991
- Union Carbide Corp. (1980). "The Acute Toxicity of MRD-80-4 to the Water Flea (*Daphnia magna* Straus)." Unpublished report.
- U.S. EPA (1989a). Study of the prenatal toxicity of Isononylalcohol 1 and Isononylalcohol 2 in rats after oral administration (gavage). EPA OTS Doc No. 89-910000247. EPA, Washington, DC, USA.
- U.S. EPA (1989b). Study of the prenatal toxicity of isodecanol, 2-ethylhexanol, and 711 alcohol (T.C.) in rats after oral administration (gavage); EPA OTS Doc No. 89-910000246.
- van Beilen JB, Eggink G, Enequist H, Bos R, Witholt B (1992). DNA sequence determination and functional characterization of the OCT-plasmid-encoded alkJKL genes of *Pseudomonas oleovorans. Mol Microbiol.* **6** (21): 3121-3136.
- Van Wezel, A.P. and A. Opperhuizen. (1995). Narcosis Due to Environmental Pollutants in Aquatic Organisms: Residue-Based Toxicity, Mechanisms, and Membrane Burdens. Critical Reviews in Toxicology 25: 255-279.
- Veith, *G.D.,* Call, D.J., and Brooke, L.T. (1983). Structure-toxicity relationships for the fathead minnow, *Pimephales promelas:* narcotic industrial chemicals. *Can. J. Fish. Aquatic* Sci., **40,** 743-8.
- Wislocki PG, Miwa GT, and Lu AYH (1980). Reactions Catalyzed by the Cytochrome P-450 System. Enzymatic Basis of Detoxification. Vol. I (ed. W.B.Jakoby), Academic Press, New York, NY.
- Zepp R and Cline D (1977). Rates of direct photolysis in the aqueous environment. Environ. Sci. Technol. **11**:359.366